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By

SUPERIOR COURT OF THE STATE OF CALIFORNIA

IN AND FOR THE COUNTY OF ALAMEDA

IN RE RANTIDINE CASES	No. JCCP 5150 No. RG20061705 (Goetz) No. 21CV002172 (Bautista) ORDER ON MOTIONS OF DEFENDANTS TO EXCLUDE EXPERT TESTIMONY (EVID CODE 801/802 AKA *SARGON/KELLY* MOTIONS) Date: 2/16/23, 2/23/23, 3/2/23, and 3/3/23 Time: Misc. Dept.: 21

The motions of defendants to exclude expert testimony came on for hearing on 2/16/23, 2/23/23, 3/2/23, and 3/3/23, in Department 21 of this Court, the Honorable Evelio Grillo presiding. Counsel appeared on behalf of Plaintiff and on behalf of Defendants. The Court, after full consideration of all papers submitted in support and opposition to the motion, as well as the oral arguments of counsel, decides as follows: IT IS HEREBY ORDERED:

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THE MOTIONS TO EXCLUDE EVIDENCE UNDER EVID CODE 801 AND 802

Defendants bring several motions under Evid Code 801 and 802 to exclude expert witness testimony at trial. The court applies the standards in *Sargon Enterprises v. University of Southern California* (2012) 55 Cal. 4th 747, and in *People v. Kelly* (1976) 17 Cal.3d 24. (See also *Bader v. Johnson & Johnson* (2022) 86 Cal.App.5th 1094, 1104-1105.)

Sargon states: "[U]nder Evidence Code sections 801, subdivision (b), and 802, the trial court acts as a gatekeeper to exclude expert opinion testimony that is (1) based on matter of a type on which an expert may not reasonably rely, (2) based on reasons unsupported by the material on which the expert relies, or (3) speculative." (*Sargon*, 55 Cal.4th at pp. 771-772.) "This means that a court may inquire into, not only the type of material on which an expert relies, but also whether that material actually supports the expert's reasoning. 'A court may conclude that there is simply too great an analytical gap between the data and the opinion proffered.'"

"The trial court's preliminary determination whether the expert opinion is founded on sound logic is not a decision on its persuasiveness. … The court does not resolve scientific controversies. Rather, it conducts a 'circumscribed inquiry' to 'determine whether, as a matter of logic, the studies and other information cited by experts adequately support the conclusion that the expert's general theory or technique is valid.' … In short, the gatekeeper's role 'is to make certain that an expert … employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field.'" (*Sargon*, 55 Cal.4th at p. 772.)

The *Sargon* phrase "based on matter of a type on which an expert may not reasonably rely" means that if a scientific professional would rely only on data or articles that met a certain

standard when doing professional work, then when that person serves as a litigation expert they can rely only on that type of matter when forming a litigation opinion.

The *Sargon* phrase "based on reasons" means that if a scientific professional would employ a level of intellectual rigor when doing professional work, then when that person serves as a litigation expert, they must employ the same level of intellectual rigor when forming a litigation opinion. (*Sargon*, 55 Cal.4th at 772.)

The *Sargon* word "speculative" appears to be a catchall that is arguably redundant. *Sargon*, 55 Cal.App.4th at 771-772, discussed *Lockheed Litigation Cases* (2004) 115 Cal.App.4th 558, and *Lockheed* used the word "speculative," so it appears *Sargon* used the word "speculative" to ensure that there was no lowering of the "speculative" standard in existing law.

In addition to *Sargon*, defendants framed some of their arguments under *People v. Kelley* (1976) 17 Cal.3d 24, which concerns whether evidence obtained by use of a new scientific method depends upon a "technique, process, or theory" that may be considered new to science and law and whether the technique, process, or theory is generally accepted as reliable in relevant scientific community. (*People v. Peterson* (2020) 10 Cal.5th 409, 444; *Bader*, 86 Cal.App.5th at 1135-1137 [concurrence].)

WHAT THE MOTIONS ARE NOT

The motions are not motions for summary judgment on the merits. A motion in limine is not a procedural vehicle for evaluating the merits of the case. (*Amtower v. Photon Dynamics, Inc.* (2008) 158 Cal.App.4th 1582, 1588, 1593-1595; *R & B Auto Center, Inc. v. Farmers Group, Inc.* (2006) 140 Cal.App.4th 327, 371 [concurring opinion].) The motions are not closing argument about whether the expert testimony is persuasive. Counsel can argue at closing

whether the jury should find the evidence to be persuasive. The motions are not a substitute for the jury weighing competing evidence. The jury has the responsibility for resolving conflicts between (admissible) competing expert opinions. (*Sargon*, 55 Cal.4th at 772.)

The motions to exclude evidence are not premature motions for non-suit, directed verdict, or judgment notwithstanding the verdict. (*Cooper v. Takeda Pharmaceuticals America, Inc.* (2015) 239 Cal.App.4th 555, 572 [noting equivalence among the motions].) If at trial the evidence supports "'mere possibility of such causation …; and when the matter remains one of pure speculation or conjecture, or the probabilities are at best evenly balanced, it becomes the duty of the court to direct a verdict for the defendant." (*Ortega v. Kmart Corp* (2001) 26 Cal.4th 1200, 1205-1205.)

Finally, the court's order that expert testimony is admissible is not a guarantee that plaintiff will have sufficient time at trial to present all the testimony from each of the multiple identified experts. The court is likely to set time limits on the trial to avoid "undue consumption of time." (Evidence Code 352; *California Crane School, Inc. v. National Com. for Certification of Crane Operators* (2014) 226 Cal.App.4th 12, 22-23.)

LEGAL ISSUE – IF AN EXPERT OPINION IS ADMISSIBLE FOR AN ISSUE, IS IT ALSO "SUBSTANTIAL EVIDENCE" FOR THAT ISSUE?

Some case law appears to equate the admissibility of expert opinion on causation with "substantial evidence" of causation. In *Cooper v. Takeda Pharmaceuticals America, Inc.* (2015) 239 Cal.App.4th 555, 574, the jury entered a verdict for plaintiff and then the trial court issued an order striking the expert testimony on causation and then granted JNOV. The Court of Appeal reversed and decided that the expert testimony on causation should have been admitted.

The Court of Appeal impliedly held that if the expert testimony met the Evidence Code 801/*Sargon* standard then it was "substantial evidence" of causation. *Chapman v. Procter & Gamble* (11th Cir. 2014) 766 F.3d 1296, 1308, affirmed the exclusion of evidence and stated: "the testimonies of these proffered experts could not establish general causation."

Other case law suggests that admissible expert opinion on causation is not necessarily "substantial evidence" of causation. *Davis v. Honeywell Internat. Inc.* (2016) 245 Cal.App.4th 477, 492, states "The aim … is not to admit only persuasive expert opinion; it is to exclude only "'clearly invalid and unreliable' expert opinion."

The issue might be unclear because a court must exclude expert opinion under *Sargon* if the opinion is "speculative" (*Sargon*, 55 Cal.4th at 770-772), a court must grant summary judgment if the evidence of causation is "speculative" (*Saelzler v. Advanced Group 400* (2001) 25 Cal.4th 763, 775, 781), and a court must grant a motion for JNOV if the evidence is "speculative" (*Ortega v. Kmart Corp* (2001) 26 Cal.4th 1200, 1205). If the word "speculative" means the same thing in all three contexts, that would suggest that if a trial judge found that opinion testimony not "speculative" for purposes of admitting the evidence, then the trial judge could not after hearing the trial testimony and the benefit of cross-examination decide that the expert opinion was "speculative" and grant a motion for nonsuit, directed verdict, or JNOV on that basis.

This trial court reads the law as being that a trial court can decide before trial that expert testimony is admissible under Evidence Code 801/*Sargon* and after trial decide that the same expert testimony is not substantial evidence that can support a judgement. First, at the most basic level, there is a distinction between whether information is admissible as evidence and whether that information can support a factual finding. The court determines whether

information is sufficiently relevant and reliable that it can be presented to the trier of fact (Evidence Code 310) and then the trier of fact determines whether that evidence meets the burden of proof (Evidence Code 312 and 500). Second, in a pre-trial motion the court decides only whether individual pieces of information are admissible as evidence, not whether the admitted evidence in the aggregate can support a factual finding. Trial judges routinely permit parties to present evidence that standing alone might not be sufficient to prove an element of a claim or an affirmative defense. Third, if a court's decision to admit evidence has the same effect as a court's determination that the evidence itself is "substantial evidence," then a motion to exclude evidence becomes a de facto motion for summary judgment. "[I]n limine motions are *not* designed to ...replace the dispositive motions." (*Tung v. Chicago Title Company* (2021) 63 Cal.App.5th 734, 758; *Blanks v. Seyfarth Shaw LLP* (2009) 171 Cal.App.4th 336, 375-376.) Fourth, on a pre-trial motion to exclude evidence the trial court is working with the motion papers and at trial the record might evolve into something else with cross-examination and contrary evidence. A trial judge could determine on the motion record that an opinion is not speculation and then on the full trial record determine that the opinion is speculation.

There are also two latent but important considerations. The first is that a defendant has every motive to present the issue of causation in the context of the admissibility of expert opinion on causation. On a motion in limine the trial court exercises discretion and the Court of Appeal reviews the trial court decision for substantial evidence and abuse of discretion. In contrast, if the defendant presents the issue of causation in the motion for summary judgment, then the trial court must take all reasonable inferences in favor of the plaintiff and the Court of Appeal reviews the trial court decision de novo. (Compare *Sanchez v. Kern Emergency Medical Transportation Corp.* (2017) 8 Cal.App.5th 146, 154 [in limine] with *Yanowitz v. L'Oreal USA,*

Inc. (2005) 36 Cal.4th 1028, 1037 [summary judgment].) The second is that a trial judge might want to avoid spending further judicial resources on a case that appears to have little merit. (*California Crane School, Inc. v. National Com. for Certification of Crane Operators* (2014) 226 Cal.App.4th 12, 19 [trial time is a valuable commodity].) This creates a temptation for a trial judge to seize on the first available procedural vehicle to resolve a case.

The court concludes that even if a trial judge permits a plaintiff to present expert opinion of specific causation the trial judge is able to later find that the admissible evidence of causation was not "substantial evidence" of causation. This permits the trial court to focus on the *Sargon* "circumscribed inquiry" regarding the admissibility of evidence (*Sargon*, 55 Cal.4th at 772) and limits the structural incentives for a court to resolve a case on an evidentiary ruling rather than on the merits.

CONSIDERATION OF FEDERAL TRIAL COURT'S MDL ORDER

The court has considered *In re Zantac (Ranitidine) Products Liability Litigation* (S.D. Fl., 2022) 2022 WL 17480906. The federal MDL order is a thorough review of similar issues on similar facts. The federal and California standards are "analogous." (*Apple Inc. v. Superior Court* (2018) 19 Cal.App.5th 1101, 1119.) The court uses the MDL order based on the persuasiveness of its analysis and as a cross-reference. That noted, the court does not find the MDL order dispositive.

The MDL order is an unpublished federal trial court order. Decisions by the lower federal courts "are neither binding nor controlling on matters of state law." (*T.H. v. Novartis Pharmaceuticals Corp.* (2017) 4 Cal.5th 145, 175.) A federal trial court order is no more

binding than a California trial court order. (E.g. *Pilliod v. Monsanto Co.* (Cal Superior 2019) 2019 WL 2158266 [trial court order on *Sargon* issues].)

The MDL Order is a discretionary decision on the exclusion of evidence. (*Kumho Tire Co., Ltd. v. Carmichael* (1999) 526 U.S. 137, 152.) Two different trial judges can review the same evidence, weigh the evidence differently, and make different decisions. Both might be affirmed on appeal. (*Mejia v. City of Los Angeles* (2007) 156 Cal.App.4th 151, 158.)

The MDL order concerned the exclusion of many experts who are different from the experts at issue in these California motions. One expert in one case might be not qualified on a topic or not have a foundation for their opinion, but another expert in another case might be qualified on the same topic and have a foundation for their opinion on that topic.

The MDL order is on appeal, but this is not material. Under California law, the court applies federal law regarding issue preclusion, and under federal law an order, once rendered, is final for purpose of issue preclusion until reversed on appeal. (*TIG Ins. Co. of Michigan v. Homestore, Inc.* (2006) 137 Cal.App.4th 749, 754 fn 3.)

LEGAL ISSUE – DISTINCTION BETWEEN FOUNDATION FOR OPINION AND OPINION ITSELF

In the order of 2/7/23, the court requested supplemental briefing on (1) the level of certainty that is required for matters that are the foundation of an expert's opinion; and (2) the level of certainty that an expert must have in their opinion for the opinion to be admissible.

The court starts with the distinction between facts and opinion. An expert can provide evidence about facts (e.g., lab tests) and can offer opinion testimony (e.g. standard of care, causation.) Although Evidence Code 801 concerns "opinion" testimony by expert witnesses,

courts use the Evidence Code 801 analysis when an expert seeks to present evidence of a fact that is "beyond common experience."

When an witness provides evidence about a fact (e.g. medical treatment, lab tests), then the expert can be a percipient witness (treating physician, coroner, etc.) or a litigation expert (measurements, laboratory tests, etc.). A second litigation expert can be asked to offer an opinion based on the assumption that the underlying facts are true (the hypothetical question). (*People v. Vang* (2011) 52 Cal.4th 1038, 1045.) A second litigation expert can base their opinion on facts presented by another litigation expert. (*Christiansen v. Hollings* (1941) 44 Cal.App.2d 332, 347 ["an expert may express an opinion based upon facts testified to by an expert, or upon tests made by other experts"]; *Mosesian v. Pennwalt Corp.* (1987) 191 Cal.App.3d 851, 862–863 ["The expert may even rely upon scientific tests performed by other experts"]; *Williams v. Volkswagenwerk Aktiengesellschaft* (1986) 180 Cal.App.3d 1244, 1260-1261 [litigation expert metallurgist could rely on report of litigation expert stress analyst that was "measurements" only, as distinguished from "opinions"].)

In contrast, when an expert provides opinion testimony (e.g., causation), then the testimony is not about a fact but rather is an opinion that assists the jury in making the ultimate finding of fact. (Evid Code 801(a).) *Sargon* and Evidence Code 801(b) suggest that if a litigation expert's litigation opinion is of the same level of quality and certainty as a professional scientific conclusion, then other litigation experts can rely on that opinion as the basis for their litigation opinions. (*Sargon*, 55 Cal.4th at 772.) This is consistent with case law that experts can rely on the opinions of other experts provided that the underlying opinions have "independent evidentiary value" and are not "speculative, conjectural or otherwise unreliable." (E.g., *Olive v. General Nutrition Centers, Inc.* (2018) 30 Cal.App.5th 804, 821.) This interpretation of *Sargon*

conflicts with case law before and after *Sargon* suggesting that one litigation expert cannot rely on the opinion testimony of another litigation expert. (E.g. *Christiansen v. Hollings* (1941) 44 Cal.App.2d 332, 347 ["It is, of course, the rule ... that the opinion of an expert cannot be predicated on the opinion of another expert"]; *Wicks v. Antelope Valley Healthcare District* (2020) 49 Cal.App.5th 866, 881-882 ["An expert may not predicate an opinion on the opinion of another expert"].)

This trial court holds as a matter of law that if a litigation expert's litigation opinion is of the same level of quality and certainty as a professional scientific conclusion, then other litigation experts can rely on that opinion as the basis for their litigation opinions. This is consistent with the text of Evidence Code 801(b) and with *Sargon*. (*Auto Equity Sales, Inc. v. Superior Court of Santa Clara County* (1962) 57 Cal.2d 450, 455.) This is sensible because a scientific quality expert opinion provided by a litigation expert in litigation is just as reliable as the same opinion provided by the same person in a peer reviewed scientific publication. The focus on the quality of the opinion protects against the problematic situation where a party could layer litigation quality opinions by having litigation quality opinions redly on other litigation quality opinions. (Order of 2/7/23 at 4-5.) Whether an expert's work is "of a type that reasonably may be relied upon by an expert" in their professional non-litigation work is a fact specific determination by the trial judge. (*Sargon*, 55 Cal.4th at 773.)

The requirement that an expert opinion must be based on matter "of a type that reasonably may be relied upon" concerns the foundation for an expert's opinion and the methodology used by the expert. (Evidence Code 802(b), *Sargon*, supra.) A litigation expert's actual opinion can be to the lesser standard of being to "a reasonable degree of scientific or medical certainty." For example, even if "Under the present state of scientific knowledge ... it is

frequently difficult to determine the nature and cause of a particular cancerous growth," a plaintiff can prove their case in civil litigation by establishing "a reasonably probable causal connection between an act and a present injury." (*Cooper*, 239 Cal.App.4th at 587.) A litigation expert is providing a litigation opinion for litigation and not for professional purposes, so the litigation opinion does not need to be "of a type that reasonably may be relied upon" for professional purposes. A litigation expert's litigation opinion only needs the level of certainty that the plaintiff must present to prevail at trial. (*Jennings v. Palomar Pomerado Health Systems, Inc.* (2003) 114 Cal.App.4th 1108, 1118.)

As relevant to his case, a litigation expert on specific causation can rely on published epidemiological studies because they are matter "of a type that reasonably may be relied upon by an expert." (Evid Code 801(b).) In contrast, a litigation expert on specific causation cannot rely on a litigation expert's litigation quality opinion about general causation.

The court does not determine in this order whether any given litigation expert may reasonably rely on the opinion of another litigation expert. To date neither party appears to have proffered expert testimony that is of the same quality and certainty of a professional scientific conclusion. The parties may nevertheless develop the facts further in the direct and cross examination of the relevant experts. The court will reserve judgment on whether any given litigation expert in this case can reasonably rely on the opinion testimony of any other litigation expert as a foundation for a litigation opinion.

LEGAL ISSUE – STATISTICAL ANALYSIS

In the order of 2/24/23, the court requested supplemental briefing on whether a statistical finding with a relative risk of 2.0 and a confidence interval of 95% is a guideline for the exercise

of discretion or is a bright line legal requirement for three separate purposes: (a) admission of evidence regarding reliability under Evid Code 801(b); (b) admission of evidence regarding confusing or misleading the jury Evid Code 352, or (3) substantial evidence to support a factual finding.

Three concepts are central to review of the statistical analysis in the epidemiological studies.

First, it is important to be comparing populations that are substantially similar except for the thing that is to be measured. In this case, the experts considered studies that compared ranitidine with non-use, with PPI blockers, and with H2RA blockers.

Second, for a study to show specific causation under a preponderance standard, the relative risk generally must exceed 2.0. *Echeverria*, 37 Cal.App.5th at fn 7 states: "epidemiological studies with relative risk estimates greater than 2.0 ("doubling the risk") are useful to the jury as support for a specific causation opinion. These cases reason "a relative risk of 2.0 implies a 50% probability that the agent at issue was responsible for a particular individual's disease. This means that a relative risk that is greater than 2.0 permits the conclusion that the agent was more likely than not responsible for a particular individual's disease." (See also *Echeverria*, 37 Cal.App.5th at fn 13 ["Numerous commentators have criticized the use of a 2.0 relative risk threshold as a prerequisite to establishing specific causation"].)

Third, the relative risk has a confidence interval or margin of error (the range where there is 95% confidence in the result). For an expert to have confidence in the relative risk, the relative risk estimate must have a confidence interval that is entirely on one side of the 1.0 mark. (*Echeverria*, 37 Cal.App.5th at 304-305.) "For a ratio to generally be helpful in a causation inquiry it must be statistically significant—it must exist completely and fully to the right or to the

left of the dotted line—and it must not include 1.0 in its confidence interval." (*In re Zantac (Ranitidine) Products Liability Litigation* (S.D. Fl., 2022) 2022 WL 17480906 at *81, 99-100.) (See also *Duran v. U.S. Bank National Assn.* (2014) 59 Cal.4th 1, 46.) (But see *Yumori-Kaku v. City of Santa Clara* (2020) 59 Cal.App.5th 385, 422-423 [affirming use of 80% confidence interval].)

Whether a litigation expert can reasonably rely on statistical analysis for a litigation opinion is a legal issue in the sense that there is case law on the issue. (*Cooper*, 239 Cal.App.4th at 593 ["By demonstrating a relative risk greater than 2.0 that a product causes a disease, epidemiological studies thereby become admissible to prove that the product at issue was more likely than not responsible for causing a particular person's disease"]).

Whether a litigation expert can reasonably rely on statistical analysis for a litigation opinion is a fact issue in the sense that it depends on what is generally accepted in the scientific community. (*Kelly, supra.*) What is generally accepted in the scientific community will change over time as tests are run, data is collected, and reports are reviewed, presented, and published. (*People v. Leahy* (1994) 8 Cal.4th 587, 605-606; *People v. Yorba* (1989) 209 Cal.App.3d 1017, 1023 ["Science, like time, marches on"].)

Whether a litigation expert can reasonably rely on statistical analysis for a litigation opinion also depends on whether the litigation expert is providing an opinion on general or on specific causation and on the expert's stated level of certainty in their opinion. For general causation, a relative risk of over 1.0 suggests increased risk, which means that an expert could rely on statistical studies showing a risk above 1.0 to support an opinion that the product or agent generally causes the disease. (*In re Lipitor (Atorvastatin Calcium) Marketing, Sales Practices and Products Liability Litigation.* (D. S.C., 2015) 150 F.Supp.3d 644, 65—651 ["a statistically

significant relative risk ratio between 1.0 and 2.0 can be used, in conjunction with the "Hill factors," to establish general causation but cannot be used, by itself, to establish specific causation"]; *Henricksen v. ConocoPhillips Co.* (E.D. Wash. 2009) 605 F. Supp. 2d 1142, 1158 [regarding general causation, "a relative risk greater than 1.0 means the product has the capacity to cause the disease" but studies be probative of *specific* causation "only if the study shows the relative risk is greater than 2.0, that is, the product more than doubles the risk of getting the disease"].)

For specific causation, if a plaintiff relies on both statistical inferences and other evidence, then a relative risk of over 1.0 but under 2.0 can be "substantial evidence" to support causation. (*Daubert v. Merrell Dow Pharms., Inc.* (9th Cir. 1995) 43 F.3d 1311, fn 16 ["A statistical study showing a relative risk of less than two could be combined with other evidence to show it is more likely than not that the accused cause is responsible for a particular plaintiff's injury"].)

For specific causation, if a plaintiff relies only on statistical inferences, then the plaintiff does not have "substantial evidence" unless there are statistical studies showing a risk ratio above 2.0 because a relative risk of over 2.0 is required to support a reliable opinion that the product or agent caused the injury in a specific person. (*Echeverria*, 37 Cal.App.5th at fn 12 ["the 2.0 relative risk threshold is typically invoked with regard to specific causation—whether the agent caused an individual plaintiff's disease"].)

Plaintiff and defendants both point to forest plots to demonstrate that multiple studies consistently show risk ratios above 1.0 (plaintiff's point), that most, if not all, studies have risk ratios below 2.0 (defendant's point), and that many of the studies have a confidence level or margin of error that crosses the 1.0 line (defendant's point). (Plaintiff Oppo at p45, DX37,

Portier Report at p36, page 882 [NDMA and bladder cancer]; DX37, Portier Report at p48, page 892 [ranitidine and bladder cancer].) For specific causation, plaintiff argues that even if no single study meets the traditional statistical standard of "statistical significance," that the aggregate effect of multiple studies that show some correlation can demonstrate general causation even if no single study meets the standard of "statistical significance." Plaintiff has support from experts Jameson, Portier, Neugut, and Boyd. (DX 5 (Jameson Depo.) at 127:2-128:7; DX 6 (Portier I Depo.) at 110:7-112:8; DX 7 (Neugut Depo.) at 60:9-65:14; DX 53 (Boyd Depo.) at 68:4-12; 345:9-346:24.) For example, Boyd testified in terms of "graded risk" rather than statistical significance. (Boyd Depo at 139, 201-202, pages 222-223.)

This court finds that the studies that have risk estimates under 2.0 or a confidence level or margin of error that crosses the 1.0 line can be matter "of a type that reasonably may be relied upon by an expert" to support an expert opinion. (Evid Code 801.) The court is determining whether the reasoning is adequate because there is "a reasonable basis for the opinion" that is not "based on a leap of logic or conjecture." "The court does not resolve scientific controversies. Rather, it conducts a 'circumscribed inquiry' …" (*Sargon*, 55 Cal.4th at p. 772.)

First, California case law permits experts to consider and rely on statistical analyses that do not have "statistical significance." (*Echeverria*, 37 Cal.App.5th at 326 and fn 12 ["Yessaian's reliance on epidemiological studies with risk estimates less than 2.0 offered additional support for her opinion"]; *Yumori-Kaku v. City of Santa Clara* (2020) 59 Cal.App.5th 385, 422-423 [affirming use of 80% confidence interval].) California case law has not adopted a bright line rule. *Echeverria* expressly did not reach this issue. (37 Cal.App.5th at 326 and fn 12 and 13.)

Second, the court is persuaded that considering data and results that do not meet the traditional tests of "statistical significance" meet the *Kelly* test of being "generally accepted as

reliable in relevant scientific community." (PX4 Amrhein article.) (*Bader*, 86 Cal.App.5th at 1179 and fn 11 [novel theory under *Kelly*].) (See also Restatement (Third) of Torts. Restatement (Third) of Torts: Phys. & Emot. Harm § 28(c)(4) (2010); Green, *et al.*, *Reference Guide on Epidemiology in Reference Manual on Scientific Evidence* (3d ed. 2011) 549, pp. 567.) The MDL order states: "The 95% confidence interval threshold for statistical significance is not a mandatory practice, … A lack of statistically significant data does not mean that medical experts have no reliable basis for inferring a causal link between a drug and adverse events .... But as many federal courts observe, 'if an expert places undue emphasis on statistically insignificant evidence, it may indicate that the expert's methods are unreliable.'" (*In re Zantac (Ranitidine) Products Liability Litigation* (S.D. Fl., 2022) 2022 WL 17480906 at *81, 99-100.)

Third, the question of whether an expert may reasonably rely on statistical analysis to support an opinion will depend on the content of the opinion, including matters such as whether the opinion concerns general or specific causation and the strength of the opinion.

That noted, the trial court can, and should, consider the statistical guidelines when it exercises discretion in determining the admissibility of expert testimony under Evidence Code 801/*Sargon*. (*Sanchez v. Kern Emergency Medical Transportation Corp.* (2017) 8 Cal.App.5th 146, 154 [discretion].) (*Echeverria*, 37 Cal.App.5th at 325 [only studies showing relative risk estimates greater than 2.0 are useful to the jury] [citing *Cooper*].)

On motions concerning the merits, the court can independently consider the statistical guidelines if the court is asked to determine whether the expert opinion is "substantial evidence" of causation. California case law regularly refers to "statistical significance" and requires "statistical significance" for a statistical conclusion to be persuasive. (*Mahler v. Judicial*

Council of California (2021) 67 Cal.App.5th 82, 127-128 [need for statistically significant disparity to create even a prima facie showing of disparate impact age discrimination].)

TRIAL AND JCCP MANAGEMENT CONSIDERATIONS

This is a complex case under CCP 3.400 that is part of a JCCP under CCP 404. The court is directed to "actively" manage the case. (Std. Jud. Admin. 3.10(a).)

The court's order on the admissibility of opinion testimony under Evidence Code 802 and *Sargon* is limited to that issue. That noted, the court is not blind to the collateral trial and JCCP management considerations.

The Goetz case alleges personal injury claims regarding whether defendants sold an unsafe product that caused injury to plaintiff Goetz. The trial is not an FDA administrative panel hearing on whether there is an elevated risk to members of the public. The court is likely to set time limits on the trial to avoid "undue consumption of time." (Evidence Code 352; *California Crane School,* 226 Cal.App.4th at 22-23.)

The JCCP includes many individual cases by plaintiffs who have similar claims. A jury verdict about the common issue of general causation might be useful if the jury verdict applied to all the cases in the JCCP. That would have an effect similar to class certification for a single issue, where a class is certified for common determination of a single issue but that resolution of other issues are left for individual trials. "If there are genuinely common issues, issues identical across all the claimants, issues moreover the accuracy of the resolution of which is unlikely to be enhanced by repeated proceedings, then it makes good sense, especially when the class is large, to resolve those issues in one fell swoop while leaving the remaining, claimant-specific issues to individual follow-on proceedings." (*Mejdrech v. Met-Coil Sys. Corp.* (7th Cir. 2003) 319 F.3d

910, 911.) (See also *Hernandez v. Motor Vessel Skyward* (S.D. Fla. 1973) 61 F.R.D. 558, 561; *In re Honda Am. Motor Co. Dealership Rels. Litig.* (D. Md. 1997) 979 F. Supp. 365.)

But this is a JCCP and not a class action. A verdict in one case might be instructive to the parties about how a jury might decide other cases, but it is entirely possible that different juries will make different factual findings after considering the same evidence relating to the same issue. "It is obvious that there can be substantial evidence to support findings either way on issues as to which evidence is conflicting." (*Jackson v. City of Pomona* (1979) 100 Cal.App.3d 438, 451.) (See also *Pilliod v. Monsanto Company* (2021) 67 Cal.App.5th 591, 621 [nature of "substantial evidence"].) In addition, the science is still developing on whether ranitidine causes bladder cancer, or other cancers.[1] Thus, any order on the admissibility of expert testimony is limited by the science that that was available to the litigation experts at the time of their litigation opinions.

OVERVIEW

The court follows the order of the causation analysis: (1) whether ranitidine degrades to NDMA outside the body, (2) whether ranitidine creates NDMA inside the body, (3) whether NDMA causes cancer (aka general causation), (4) whether Goetz consumed ranitidine that exposed him to meaningful doses of NDMA, and (5) whether the NDMA from ranitidine caused Goetz to develop bladder cancer (aka specific causation). The court ends with regulatory matters related to duty and breach.

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[1] In the hearings in the motions, counsel referred to the newly published Joung (2022) study. " A common refrain in *Daubert* jurisprudence is that "law lags science," because the courtroom is not the appropriate forum for new scientific methodologies and theories to be tested; laboratories and published journals are the appropriate forum." (*In re Zantac (Ranitidine) Products Liability Litigation* (S.D. Fl., 2022) 2022 WL 17480906 at *3.)

BENET

The Motion of Defendants to exclude certain testimony of Benet is DENIED.

Benet is a pharmacologist, which means he studies the interactions between drugs and humans. Benet prepared a report. (DX 122, Benet Report.) Benet was deposed. (DX 9, Benet Depo.)

Benet states he was asked to address four general topics, several of which have subparts. (DX 122, Benet Report at 8-9; pages 3083-3084.)[2] Defendant's motion is directed at fewer than all of the topics.

Benet MAY offer an opinion about the manufacturing and pharmacokinetics (absorption, distribution, metabolism and excretion) of ranitidine. Benet's opinion is based on matter on which an expert would reasonably rely. Benet's reasoning supports his conclusions. (Benet Report at 9-12 pages 3084-3087.)

Benet MAY offer an opinion about the pharmacokinetics (absorption, distribution, metabolism and excretion) of NDMA. Benet's opinion is based on matter on which an expert would reasonably rely. Benet's reasoning supports his conclusions. (Benet Report at 12-16, pages 3087-3061.)

Benet MAY offer an opinion that NDMA has many of the characteristics of agents that are known to cause cancer. The Benet Report states Benet was asked to address: "How NDMA is believed to mechanistically cause cancer. (1) Of the ten known characteristics of carcinogens, which of these does NDMA activate and why this is relevant." (DX 122, Benet Report at 8, para

[2] The court refers to evidence as PX or DX, then an identification, and then for the DX exhibits the page number of the Defendants' Compendium of Evidence, which is 4161 pages long.

14.C; pages 3083.) Benet reviewed an IARC publication that identified 10 key characteristic that are commonly exhibited by established human carcinogens, and then compared those to NDMA. (Benet Report at 16-18.) Benet's opinion is based on matter on which an expert would reasonably rely. Benet's reasoning is adequate. (Benet Report at 16-18 pages 3061-3063.)[3]

Benet MAY offer an opinion on how ranitidine degrades into NDMA with exposure to heat and over time. Benet relied on the GSK Root Cause (King) study (2020) and the Abe (2020) study. Both concerned out of the body (exogenous) formation.

Benet MAY offer an opinion on how ranitidine creates NDMA in the body. The Benet Report states Benet was asked to address: "How ranitidine breaks down to NMDA … (4) In the human body." (DX 122, Benet Report at 8, pages 3083-3084.) Benet considered several studies, including the HHS draft Toxicological profile for NDMA, the De Flora (1983) study, the Gao (2021) study, the Mitch study, the Florian (2021) study. (DX 122, Benet Report at 22-24, pages 3097-3099.)

Benet considered the HHS draft Toxicological profile for NDMA. (DX 122, Benet Report at 12-13, page 3087-3088.) The HHS draft Toxicological profile states: "For most people, the largest source of exposure to NDMA is through endogenous production (within the body) from precursors (presence of nitrite in foods including drinking water) that occur naturally in the body or in the diet. External sources of NDMA exposure include foods and malt beverages, water, cigarette smoke, and to a lesser extent rubber products, toiletry and cosmetic products, and pesticides. In addition, some people may have had exposures to NDMA through

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[3] GSK may cross-examine Benet on the significance of meeting the factors. For example, when asked at deposition about whether there are any studies about the significance of meeting one or seven of the categories, Benet responded, "I don't know. It's not my field."

the use of contaminated medications." (DX 113, draft Toxicological Profile p1, page 2967.)[4] Benet's opinion is based on matter on which an expert would reasonably rely.

Benet considered and distinguished the Florian (2021) study. (DX 122, Benet Report at p19-24, pages 3094-3099.) The Florian study found "In this randomized, placebo-controlled study in healthy participants, oral administration of ranitidine (300 mg) did not significantly increase 24-hour urinary excretion of NDMA" and concluded "These findings do not support that ranitidine is converted to NDMA in a general, healthy population." Benet distinguished the Florian study on the basis that "measures of NDMA in urine do not reflect actual NDMA formation in the body." (DX 122, Benet Report at p15, page 3090.) (See also DX 122, Benet Report at p23-24, page 3098-3099.) The Florian study also reviewed various other studies and concluded "no consistent signals emerged across studies, and studies with comparison to active controls found no association between ranitidine and overall or specific cancer risk." (DX 60, Florian at 246-247, page 1973-1974.) Benet separately considered the various other studies.

Benet considered the De Flora study and relied on that study. (DX 122, Benet Report at p22)

Benet disagreed with the Gao study. (DX 122, Benet Report at p22) Benet notes the Zeng & Mitch (2016) report and that it was retracted. (DX 122, Benet Report at p22-23.)

Benet's opinion is based on matter on which an expert would reasonably rely. Benet's opinion is based on an appropriate level of intellectual rigor. Benet reviews the studies of others, has critical analysis, and then states opinions.

In considering whether Benet's reasoning supports his conclusions, the court also considered the strength of Benet's conclusions. Some of Benet's conclusions are equivocal and simply state what is possible and what can or what could occur. Benet's report at p23 states: "there is no convincing justification to assume that urinary measures of NDMA in humans or

[4] The HHS draft Toxicological Profile is a draft.

animals either support or negate conclusions as to the extent of NDMA formation." Benet's report at p23 states: "I will only conclude that it is *possible* for NDMA formation from ranitidine to also result from reaction in the gastrointestinal tract following oral administration of ranitidine formulations." Benet's report at p26 states: "I have provided the hypothesized mechanisms for NDMA breakdown in the human body and the *potential* toxic byproducts that can occur." Benet's report at p26 states that he detailed: "the *possibility* that NDMA could be formed in the stomach of humans but be modified by meals." Because Benet limited his opinion to "potential" or "possibility" level of certainty, the *Sargon* analysis of that opinion concerns whether his reasoning supports an opinion at that level of certainty.

BOSE

The Motion of Defendants to exclude testimony of Bose is GRANTED IN PART.

Bose is an analytical/bioanalytical chemist, which means he tests drugs and chemicals. Bose prepared a report. (DX 36, Bose Report.) Bose was deposed. (DX 17, 18, Bose Depo.)

The Bose Report contains information on the content of NDMA in tablets identified as Bautista, Eiss, Goetz, Pratt, Riggio, Russell, and Warwick. (DX36, Bose Report at section 7, pages 840-841.) Defendant's motion is directed at the analytical methods for the tests and whether they can be used to estimate how much NDMA Goetz ingested. (Najafi/Bose Motion p1)

The Bose Litigation Testing evaluated four of Mr. Goetz's ranitidine-containing pills that Emery Pharma received from Plaintiffs' counsel. None of Mr. Goetz's samples were brand-name Zantac. All of Mr. Goetz's samples were expired.

LITIGATION TESTING METHODOLOGY

Defendants argue that the ligation testing did not use generally accepted methods. This is either a *Sargon* based on matter "of a type that reasonably may be relied upon by an expert" argument or a *Kelly* argument.

Bose MAY offer the results of Emery Pharma's litigation testing of the four Goetz pills. Bose is Chief Scientific Officer of Emery Pharma and oversees the testing and may offer the testing even though he did not personally conduct the testing. For the litigation testing, Emery used Hydrophilic Interaction Liquid Chromatography (HILIC) rather than liquid chromatography-tandem mass spectrometry (LC-MS/MS) for the first phase of the test process. HILIC is an established and accepted chemistry method for the retention and separation of polar compounds such as NDMA. (Olson Monograph, PX 67 at 8, 138, 143, 225.)

GSK argues that the HILIC testing is unreliable because Emery Pharma is the only lab that has used HILIC and all of the other testing of ranitidine was done with liquid chromatography-tandem mass spectrometry (LC-MS/MS). This does not mean that the HILIC method is improper or that it is not an accepted method. It just means that Emery Pharma used an established testing procedure in a different factual situation. (*Roberti v. Andy's Termite & Pest Control, Inc.* (2003) 113 Cal.App.4th 893, 901-902.)

USE OF LITIGATION TESTING TO ESTIMATE GOETZ'S INGESTION OF NDMA

Defendants argue that the ligation testing cannot assist the trier of fact in estimating Goetz's ingestion of NDMA. This is an Evidence Code 801 "assist the trier of fact" argument.

Bose may NOT testify about the levels on NDMA in the pills taken by Goetz. Plaintiff's opposition states: "neither Dr. Bose nor Dr. Najafi are giving any specific cause opinion as to

how much NDMA Mr. Goetz was exposed to from consuming ranitidine." (Oppo at 97:7-8.) Plaintiff's opposition states: "Neither Dr. Bose nor Dr. Najafi seeks to opine as to the levels of NDMA in any pills taken by Mr. Goetz at the time he ingested them—that would be impossible." (Oppo at 97:22-25.)

Bose MAY testify that the Bose report measured the NDMA in four of Goetz's pills and to state the result of the litigation tests. The Emery Pharma test results of Goetz's pills are expert scientific measurements rather than expert opinions. Defendants can cross-examine and argue that the tested pills are generic pills that were expired at the time of the tests and the test results do not permit even informed speculation about the level of NDMA in Goetz's branded ranitidine when he consumed his pills.

The litigation test results of Goetz's pills are relevant and will assist the trier of fact. (Evidence Code 801.) First, the product is off the market and the product degrades over time, so the only way to test Goetz's pills is to test the expired generic pills that were in his possession. Second, the generic pills are supposed to be chemically the same as the branded pills, so there is a reasonable inference that the test results for Goetz's generic pills would mirror the results of his branded pills.[5] Defendant GSK may cross-examine and argue about whether Emery Pharma tests of expired generic pills are probative of the amount of NDMA that was in the branded pills that Goetz consumed.

Bose MAY testify that the Bose report measured the NDMA in the pills of various non-Goetz plaintiffs and to state the result of those litigation tests. The Emery Pharma tests of the pills of the various non-Goetz plaintiffs are arguably not a reliable sample because they are not the tests of randomly selected pills. That noted, the tests of the pills by various more established

organizations were also not reliable samples because they were also not the tests of randomly selected pills. Those entities include the FDA, Health Canada, the Australian Therapeutic Goods Administration (TGA), the Saudi Food & Drug Authority; GSK, Sanofi, and Abe (2020). (Defendant's moving brief on Najafi and Bose, page 27 [table].) If the more established organizations tested pills that were not selected at random and considered the results for their decisions, then Bose may rely on Emery Pharma's tests of pills that were not selected at random and consider the results for his opinions.

NAJAFI

The Motion of Defendants to exclude testimony of Najafi is GRANTED IN PART.

Najafi is an organic chemist who worked in the pharmaceutical industry and now is CEO of Emery Pharma. Najafi prepared a report. (DX 39, 40, Najafi Report.) Najafi was deposed. (DX 11, 12, Najafi Depo.) Najafi was asked to address several topics. (DX 39, Najafi Report at para 9-10, pages 972-973; DX 40 at pages 1165-1188.) Defendant's motion is not directed to all aspects of Najafi's opinions. (Najafi/Bose Motion p1)

EMERY PHARMA TESTING OF RANITIDINE FOR BASELINE NDMA

Emery Pharma received pills for litigation testing. Emery tested 254 batches in total, 166 of them were not expired and 88 were expired. (DX 39, Najafi Report para 130, page 1031) Najafi reviewed the results of the Emery Pharma testing. Najafi Report attaches the Bose Report as Exhibit A. Najafi relied on the data in the Bose Report.

[5] Defendant presented contrary evidence that the branded pills had considerably less NDMA than the generic pills.

Najafi MAY rely on the Emery Pharma tests of baseline NDMA even though he did not personally review the chromatograms of the NDMA. Najafi is CEO of Emery Pharma and oversees the testing and may review and offer opinions about the results of the chromatograms even though he did not personally conduct the testing.

Najafi MAY rely on the Emery Pharma tests of the 254 batches of pills to determine baseline NDMA (the Bose Report). The Emery Pharma tests of the 254 batches of pills are matter "of a type that reasonably may be relied upon by an expert." The Emery Pharma lab tests were not lab tests of randomly selected pills. That noted, the tests of the pills by various more established organizations were also not reliable samples because they were also not the tests of randomly selected pills. Those entities include the FDA, Health Canada, the Australian Therapeutic Goods Administration (TGA), the Saudi Food & Drug Authority; GSK, Sanofi, and Abe (2020). (Defendant's moving brief on Najafi and Bose, page 27 [table].) If the more established organizations tested pills that were not selected at random and considered the results for their decisions, then Najafi may consider Emery Pharma's tests of pills that were not selected at random and consider the results for his opinions.

NAJAFI OPINION ABOUT RANITIDINE CONSUMED BY GOETZ

Najafi will NOT be permitted to testify that the Emery Pharma testing estimates Goetz's ingestion of NDMA. Najafi does intend to offer that opinion. (See discussion above regarding Bose)

NAJAFI OPINION ABOUT BASELINE RANITIDINE

Najafi MAY provide opinion testimony about baseline ranitidine.

Najafi MAY testify about the results of the Emery Pharma testing on the 254 batches of pills. Najafi concluded "Emery's baseline testing of ranitidine drug substance and Zantac finish dose tablets found NDMA in all samples tested." (Najafi Report paras 127-136, DX pages 1030-1035.) The Emery Pharma lab tests on the 254 batches of pills are matter on which an expert would reasonably rely. Najafi's reasoning is adequate.

Najafi MAY testify about the baseline NDMA based on testing by the FDA and peer reviewed scientific reports. (E.g. Najafi Report para 19, DX pages 978-979 [Najafi discussing FDA report on NDMA impurities].) Najafi's reasoning is adequate.

NAJAFI OPINION ABOUT RANITIDINE DEGRADING IN HEAT AND HUMIDITY

Najafi MAY provide opinion testimony the ranitidine can degrade to NDMA in heat and humidity.

Emery Pharma conducted testing designed to mimic real-life storage conditions of pills, including storage conditions such as ranitidine tablets being stored in the bathroom, car (sun or shade) as well as storage in four climatic zones. Najafi has the opinion that when exposed to heat and humidity "significant levels of NDMA can form in addition to any starting baseline levels of NDMA in the tablets." (DX39, 40, Najafi Report at para 10(d) and 244-260; page 973, 1083-1093.) (See also Najafi Report at para 261-273 [degradation in similar drugs].) Najafi also considered the GSK's Root Cause Analysis (aka King study). (DX 38, Najafi Report at 30-33, pages 998-1001.) GSK's Root Cause Analysis found that ranitidine degrades over time and that heat and humidity contribute to the rate of degradation. (DX 73, King study, pages 2140-4161.)

Najafi MAY rely on the Emery Pharma tests of storage conditions. Emery Pharma's testing used accepted scientific methods to test whether ranitidine degraded under certain temperature and humidity conditions. These tests are "of a type that reasonably may be relied upon by an expert." Defendant's argument is in large part a *Kelly* argument that there is no established protocol how to determine whether ranitidine degrades under certain temperature and humidity conditions. That might be true, but in the absence of any established protocol on that specific issue it just means that Emery Pharma used an established testing procedure in a different factual situation. (*Roberti v. Andy's Termite & Pest Control, Inc.* (2003) 113 Cal.App.4th 893, 901-902.)

Najafi MAY rely on the Emery Pharma tests as a basis for his opinion that ranitidine degrades under certain temperature and humidity conditions on a range of conditions. Defendant's argument that the Emery Pharma tests are not based on real world examples is a relevance and usefulness argument under Evid Code 351 and 801(a). The Emery Pharma tests are relevant and useful. Defendants may cross examine and argue that the Emery Pharma tests do not reflect real world scenarios. Defendants may present their own experts with information about what they consider to be real world scenarios.

NAJAFI OPINION THAT RANITIDINE CAN CREATE NDMA IN THE BODY

Najafi MAY provide opinion testimony that ranitidine can create NDMA in the body.

Emery Pharma conducted testing on ranitidine (DX 39, Najafi Report, para 163-170), Najafi reviewed the simulated gastric fluid studies of Valisure, Braunstein, and Gao (Najafi Report at para 171-184), Emery Pharma conducted simulated gastric fluid studies without food (Najafi Report at para 185-194), Emery Pharma conducted simulated gastric fluid studies with

food (Najafi Report at para 195-215), and Najafi considered the Florian Study of a clinical trial (Najafi Report at para 216-227). Najafi has the opinion that "ranitidine can cause NDMA to form endogenously by its interaction with nitrites in food and gastric fluid." (Najafi Report at para 10(e) and 163-234; page 973, 1046-1080.)

Najafi MAY rely on the Emery Pharma tests for his opinion on whether ranitidine creates NDMA in the body either with or without food. The Emery Pharma tests are matter "of a type that reasonably may be relied upon by an expert." The range of conclusions in the published literature and in the Emery Pharma testing of simulated gastric fluid indicate that the science is still very much in development. Najafi's opinion was consistent with the current state of the science. Consistent with the scientific uncertainty, Najafi's opinion is the general statement that "ranitidine can cause NDMA to form endogenously by its interaction with nitrites in food and gastric fluid." (Najafi Report at para 10(e); page 973.)

GENERAL CAUSATION – OVERVIEW

General causation concerns whether there is a reasonable scientific basis for concluding that use of ranitidine increases the risk of bladder cancer in humans. (*Echeverria,* 37 Cal. App. 5th at 297.) General causation is a subject that "is sufficiently beyond common experience that the opinion of an expert would assist the trier of fact." (Evid Code 801(a).) The general causation experts are Portier, Neugut, Jameson, and Benet.

"Three types of data are widely accepted as being relevant to determine whether a substance causes cancer: human cancer data (the realm of epidemiology…), experimental animal data, and mechanism data [how a substance is absorbed and metabolized]." (*Pilliod v. Monsanto Company* (2021) 67 Cal.App.5th 591, 602.) An expert can reasonably consider all three

categories of data. That noted, the three types of data are not equivalent regarding the issue of whether ranitidine causes cancer in humans.

Epidemiological data is a one-step measurement of whether the use of ranitidine correlates with an increase in cancer in humans. Epidemiological studies can consider dose and exposure levels, confounding factors, statistical significance, and other variables and evaluate whether any correlation suggests causation. Experts Neugut, Portier, and Jameson rely on epidemiological studies.

Animal data and mechanism data are different because they are each steps in a multi-step process to evaluate whether the use of ranitidine causes cancer in humans. An expert must consider whether ranitidine degrades into NDMA outside the body through heat, humidity, time, or other factors, the NDMA doses created by degradation, whether ranitidine creates NDMA inside the body, whether NDMA has a mechanism to create cancer, whether NDMA causes cancer in animals, what dose of NDMA causes cancer in animals, what dose of NDMA causes cancer in humans, and whether that supports a conclusion that the use of ranitidine in humans at normal doses suggests an increase in cancer in humans. Portier and Jameson rely on animal data. Portier, Jameson, and Benet rely on mechanism data.

LEGAL ISSUE – IMPORTANCE OF DOSE FOR GENERAL AND SPECIFIC CAUSATION

The dose is an important part of any causation analysis because "[a] fundamental tenet of toxicology is that the dose makes the poison' and that all chemical agents, including water, are harmful if consumed in large quantities, while even the most toxic substances are harmless in minute quantities." (*People v. Brown* (Cal. 2023) 2023 WL 2319306 at *7.) An expert, and the trier of fact, must "consider the relationship between dose and response, the shape of the dose-

response curve at lower levels of exposure, and the possibility that exposure may not cause a disease when the exposure is below a threshold level." (*Lockheed Litigation Cases* (2005) 126 Cal.App.4th 271, 23 Cal. Rptr. 3d 762, 779 [superseded].)[6]

GSK implicates the issue of dose when it argues that plaintiff's experts cannot reasonably rely on epidemiology studies (rubber worker and dietary) that examine whether NDMA causes cancer because there is no reliable way to compare the fluctuating dose of inhaled NDMA in a rubber factory with the suggested dose of NDMA in degraded ranitidine. This is intertwined with GSK's argument that the experts cannot examine the ingredient (NDMA) in isolation and must examine the ingredient (NDMA) as it is incorporated into and consumed in the product (ranitidine). GSK cites to four cases.

Lockheed Litigation Cases (2005) 126 Cal.App.4th 271, 23 Cal. Rptr. 3d 762,[7] affirmed a trial judge's discretionary decision to exclude an expert on general causation because the expert relied on multi-solvent studies and "epidemiological studies involving exposure to many solvents cannot support a reasonable inference that a particular solvent contributed to the reported injuries." (23 Cal. Rptr. 3d at 768.) The Court of Appeal held that the expert's reliance on "epidemiological studies show[ing] that persons exposed to many solvents suffered a greater incidence of disease than persons not exposed" was not a reasonable basis for the expert's

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[6] Counsel discussed case law on asbestos, but the case law on the exposure to asbestos is confined to asbestos because of factors unique to asbestos. *Davis v. Honeywell Internat. Inc.* (2016) 245 Cal.App.4th 477, 492-493, states: "*Rutherford* does not require a "dose level estimation." ... a plaintiff may satisfy this requirement through the presentation of expert witness testimony that "each exposure, even a relatively small one, contributed to the occupational 'dose' and hence to the risk of cancer." For other agents, "the dose makes the poison" and a plaintiff must provide evidence of the dose.

[7] *Lockheed Litigation Cases* (2005) 126 Cal.App.4th 271, 23 Cal. Rptr. 3d 762, 769, 774, was superseded, is not binding precedent, and arguably should not be cited. (CRC 8.1100(e) and 8.1115(e).) The court considers it because the parties discussed it and because it is the only California appellate authority on this issue.

opinion because the multiple-solvent studies did not permit an opinion on "whether persons exposed to only the solvents at issue here suffered a greater incidence of disease than persons not exposed." (23 Cal. Rptr. 3d at 774.) Stated otherwise, the multiple-solvent studies did not permit the expert to reasonably opine that the particular agent in the exposure dose caused the relevant injury.

Chapman v. Procter & Gamble (11th Cir. 2014) 766 F.3d 1296, 1308, affirmed the trial judge's discretionary decision in *In re Denture Cream Products Liability Litigation* (S.D. Fla. 2011) 795 F.Supp.2d 1345, to exclude experts on general and specific causation because the experts did not consider the dose and duration of Fixodent use that might cause the injury and failed to consider the background rate of the injury. The *Chapman* opinions do not clearly address the distinctions between whether zinc causes the injury, whether the zinc in Fixodent can generally cause the injury, and whether the zinc in Fixodent at the dose used by plaintiff specifically caused plaintiff's injury. More importantly, the *Chapman* opinions seem to equate the evidence issue of scientific reliability with the merits issue of whether the evidence could support a judgment for the plaintiff. The focus on the merits is apparent when the trial court stated: "Hypotheses are verified by testing, not by submitting them to lay juries for a vote. It may very well be that Fixodent in extremely large doses over many years can cause copper deficiency and neurological problems, but the methodology [the Chapmans'] experts have used in reaching that conclusion will not reliably produce correct determinations of causation." (796 F.Supp.2d at 1367; 766 F.3d. at 1311-1312.)

Henricksen v. ConocoPhillips Co. (E.D. Wash. 2009) 605 F. Supp. 2d 1142, concerned causation and highlighted the issue of whether the case was about exposure to gasoline (defendant's product) or exposure to the benzene that was included in the gasoline. (605 F.

Supp. 2d at 1155-1156.) The trial judge excluded "all the Plaintiffs' general causation experts ... based upon their reliance upon allegedly unreliable or irrelevant epidemiological studies." (605 F. Supp. 2d at 1168.) The *Hendrickson* opinion's concern with measuring benzine or measuring benzine in gasoline is based on the difficulty of measuring dose when the benzine is part of another product. *Hendrickson* does not suggest that an expert cannot measure the impact of an agent whenever it is part of another product. The *Hendrickson* opinion also seems to equate the evidence issue of scientific reliability with the merits issue of whether the evidence could support a judgment for the plaintiff.

Burst v. Shell Oil Co. (E.D. La. 2015) 2015 WL 3755953, is in large measure a repeat of the analysis in *Hendrickson*. The trial judge excludes the testimony of an expert on whether benzine in gasoline causes AML because the expert relied primarily on benzine studies, did not give adequate weight to the gasoline studies, and did not have a reasonable methodology for his analysis.

The court does not read the above four cases as suggesting that an expert cannot consider the potential harmfulness of an ingredient in isolation and can only consider the ingredient (NDMA, benzene, etc.) as an ingredient in the product that is delivered to customers (ranitidine, gasoline, etc.).

The court reads the above cases as focusing on the difficulties of determining the dose of an ingredient when it is part of another product. The dose is an important part of any causation because "the dose makes the poison." (*People v. Brown* (Cal. 2023) 2023 WL 2319306 at *7.)

On general causation, an expert must determine what dose generally causes injury. On specific causation an expert must have information about plaintiff's exposure to some dose before the expert can opine that the ingredient caused the injury to the specific plaintiff. The

above four cases do not suggest that experts cannot consider studies on NDMA and must rely only on epidemiology studies regarding ranitidine. The cases do highlight that any experts on causation must have information about the dose before they can offer an opinion about whether a particular dose causes injury generally or caused injury to the plaintiff specifically.

NEUGUT

The Motion of Defendants to exclude testimony of Neugut is DENIED.

Neugut is an epidemiologist and oncologist. Neugut prepared a report. (Neugut Report DX 120, 121, pages 3038-3073.) Neugut was deposed twice. (Neugut Depo at DX 5, 6) (See also Neugut Depo in other case DX 127].)

Neugut was "asked to assess whether ingestion of ranitidine, contaminated with NDMA, is causally associated with the development of urinary bladder cancer." (DX 120, Neugut Report at p4, page 3042.) Neugut's opinion is that "to a reasonable degree of scientific certainty, the ingestion of ranitidine, and NDMA contained therein, can cause development of urinary bladder cancer." (DX 120, Neugut Report, page 3042.)

Neugut's opinion is based on epidemiology. Neugut reviews principles of epidemiology (DX 120, Neugut Report at 4-10, page 3042-3048), the multi-causal phenomena (DX 120, Neugut Report at 11-12, page 3049-3050), the Bradford-Hill criteria for evaluating when correlation suggests causation (DX 120, Neugut Report at 12-14, page 3050-3052), and the complications that can affect analysis (DX 120, Neugut Report at 16-19, page 3054-3056). Neugut then turns to the analysis as applied to this case.

Neugut considered occupational studies (DeVocht – rubber tire plant (2009), Hidajat – rubber factories (2019), Straif – rubber factories (2000), Vlaanderen – tire factories (2013) and

red meat intake studies Jakszyn, Rinco, Crippa, Dianatinasab). Neugut considered studies about ranitidine and bladder cancer (Habel (2000), Cardwell (2021), Pottegard (2018), Kantor (2021), McDowell (2021), Yoon (2021), Norgaard (2022). Regarding Habel (2000), Neugut said "I will acknowledge that it is a relatively weak contributor. I wrote as much in my report." (DX8, Neugut Depo at 128, page 147.)

Neugut applied the Bradford-Hill criteria and concluded "it is my expert opinion, within a reasonable degree of medical certainty, that there is a causal association between ranitidine and urinary bladder cancer." (DX 120, Neugut Report at p26-27; pages 3064-3065.)

Neugut MAY reasonably rely on Hidajat (2019), which studied workers in UK tire plants. Hidajat showed correlation between exposure to NDMA and bladder cancer. (DX 120, Neugut Report at p19-20; pages 3057-3058.) The Hidajat rubber worker study is a matter "of a type that reasonably may be relied upon by an expert" evaluating whether *NDMA* causes bladder cancer. In contrast, the Hidajat rubber worker study is not a matter "of a type that reasonably may be relied upon by an expert" evaluating whether *ranitidine* causes cancer.

The parties disputed whether Hidajat retracted some or all of her opinion. The Hidajat testimony indicates that Hidajat did not retract her opinion that NDMA likely causes cancer. The court has read the Hidajat deposition excerpts and a few things are clear: (1) counsel for plaintiffs in the MDL retracted any intent to use Hidajat, stating: "Dr. Hidajat is not going to be offered as an expert to testify at trial that NDMA or ranitidine causes cancer" (Depo at 46:8-10) (See also Depo at 43: 1-4); (2) Hidajat did not study consumption of ranitidine by rubber workers (Depo at 54:1-2 and 22-24); (3) Hidajat did study exposure to NDMA in rubber workers (Depo at 54:16-19); (4) Hidajat found a relationship between NDMA exposure and cancer (Depo at 143:8-13), and (5) Hidajat thought that more study was necessary before extrapolating

her findings to other circumstances (Depo at 142-144). The Hidajat deposition testimony also indicates that Hidajat frequently begins her sentences with "yes" or "yeah" to acknowledge the question the way other people might begin sentences with "okay," "um" or "well" before she gets to the content of her answer.

Neugut MAY reasonably rely on deVocht (2009), which studied workers in a Polish rubber tire plant and Straif (2000), which studied workers in German rubber plants. These showed correlation between exposure to NDMA and bladder cancer. (DX 120, Neugut Report at p19-20; pages 3057-3058.) These rubber worker studies are matter "of a type that reasonably may be relied upon by an expert" evaluating whether NDMA causes bladder cancer. As with Hidajat, these studies do not study or concern a relationship between ranitidine and cancer.

Neugut MAY reasonably rely on the epidemiological studies of dietary NDMA (red/processed meats) to determine whether NDMA at certain doses causes cancer in humans. Neugut considered Jakszyn (2011), Ronco (2014), Crippa (2018), and Dianatinasab (2021). These showed correlation between exposure to NDMA and bladder cancer. (DX 120, Neugut Report at p20-21; pages 3058-3059.) These dietary studies are matter "of a type that reasonably may be relied upon by an expert" evaluating whether NDMA causes bladder cancer. Again, these studies do not study or concern a relationship between ranitidine and cancer.

The court has considered the discussion of the rubber worker studies and the dietary studies in the MDL order. *In re Zantac (Ranitidine) Products Liability Litigation* (S.D. Fl., 2022) 2022 WL 17480906 at *100-112.) The federal judge in her discretion concluded that there was too great an analytical gap from exposure to NDMA in rubber factories or through diet, to ranitidine forming NDMA, to there being some dose of NDMA in the plaintiff, to the NDMA causing cancer in the plaintiff. This trial judge reads the Neugut report as relying on the

rubber worker studies and the dietary studies only for an opinion that NDMA causes cancer and not for an opinion that ranitidine causes cancer, and certainly not for an opinion that ranitidine caused cancer in Goetz.

Neugut MAY reasonably rely on the published epidemiological studies of Ranitidine v. Non-Use, Ranitidine, v PPIs and Ranitidine v. H2RA. (DX 121 [Dr Neugut's Forest Plot log scale].) Those studies are "of a type that reasonably may be relied upon by an expert."

Neugut's reasoning MAY be the basis for his opinion on general causation. Neugut's Bradford-Hill analysis is "based on reasons supported by the material on which the expert relies." Neugut is an epidemiologist and he walks through the Bradford-Hill analysis.

Regarding what to compare, Neugut testified that the studies that evaluate Ranitidine v. H2RA are generally better than the studies that evaluate Ranitidine v. Non-Use or Ranitidine v. PPIs. (Neugut depo at 98-99, 119-120), but he also qualified that by stating that they are "a little better, not dramatically better" (Neugut Depo at 387). Regarding the studies, Neugut's forest plot shows that in comparisons between ranitidine and non-use, PPIs, and H2RA blockers that all of the studies have a risk ratio above 1.0 and several have confidence levels that do not cross the 1.0 line. (DX 121, page 3073.)

This implicates two of the legal issues. First, Neugut is an expert on general causation, not specific causation, so the risk ratios of consistently above 1.0 support his conclusion that NDMA creates an increased risk of bladder cancer. The 2.0 risk ratio for statistical significance applies only to the analysis of specific causation. (*Henricksen v. ConocoPhillips Co.* (E.D. Wash. 2009) 605 F. Supp. 2d 1142, 1158.) Second, the 95% confidence interval (the forest plot staying to the right of 1.0) is in the nature of a guideline and not a bright line legal requirement. (*Yumori-Kaku v. City of Santa Clara* (2020) 59 Cal.App.5th 385, 422-423 [affirming use of 80%

confidence interval].) Neugut testified that statistical analysis is moving away from the binary question of whether there is statistical significance and toward an analysis of association or increased risk. (PX 7, Neugut Depo at 61-65, 70-71.)

In considering whether Neugut's reasoning supports his conclusions, the court also considers the strength of Neugut's conclusions. Neugut states in his deposition that he holds his general causation opinion that ranitidine causes cancer in humans to a "reasonable level of medical certainty" which is the civil litigation 51% burden of proof, but that he probably could present or publish it in his professional capacity. (DX 5, Neugut depo at 24-26 [generally], 72-73 [statistics].) Neugut confirmed in deposition in another case that his understanding was that the litigation standard of "within a reasonable degree of medical probability" was different from and less certain than the academia or medical practice standard. (DX 127 [Neugut depo in other case].) Because Neugut limited his opinion to the civil litigation standard of "reasonable level of medical certainty," the *Sargon* analysis concerns whether his reasoning supports an opinion at that level of certainty.

PORTIER

The Motion of Defendants to exclude testimony of Portier is DENIED.

Portier is a biostatistician. Portier prepared a report. (Portier Report DX 37, pages 845-944.) Portier was deposed. (DX 2, pages 193-206.)

Portier was asked to evaluate whether "ranitidine could be causing various cancers in humans who have used [ranitidine]." Portier applied a two-step analysis of (1) whether ranitidine is converted into NDMA either during transport / storage (exogenously) or in the body (endogenously) and (2) whether NDMA that is a carcinogen that causes various cancers in

humans, considering epidemiology, animal studies, and application of the Bradford-Hill causality analysis. (DX 37 at p6-7, page 850-851.) Portier's opinion is: "In my opinion, ranitidine exposure causes bladder cancer." (DX 37 at 70, page 914.)

Portier's opinion that ranitidine degrades to NDMA during transport/storage out of the body (exogenous) (1) is supported by information "of a type that reasonably may be relied upon by an expert" and (2) is based on adequate reasoning. Portier relies on a peer reviewed published study that suggests that ranitidine degrades to NDMA in heat and humidity. (DX 37 at 67, 74, page 911, 918, referring to PX 19, Abe (2020) ["Temperature-Dependent Formation of N-Nitrosodimethylamine during the Storage of Ranitidine Reagent Powders and Tablets"].)

Portier's opinion that ranitidine creates NDMA in the body (endogenous) (1) is supported by information "of a type that reasonably may be relied upon by an expert" and (2) is based on adequate reasoning. Portier relies on several studies. (DX 37 at 67, 74, page 911, 918, referring to fn 38 [Valisure petition], fn 64 [Braunstein 2021], fn 77 [Matsuda], fn 458 [de Flora].) Some of the studies are questionable sources. The Valisure petition is not a peer-reviewed published study. Braunstein (2021) is a preprint, which means it has not been subject to peer review. Other studies are peer reviewed published studies that suggest that ranitidine creates NDMA in the body. (Matsuda (1990), de Flora (1983).)

Portier MAY reasonably rely on the published epidemiological studies of NDMA exposure and bladder cancer. (DX 37 at 38, page 882). Portier MAY reasonably rely on the published epidemiological studies of ranitidine use and bladder cancer. (DX 37 at 48, page 892). Those studies are "of a type that reasonably may be relied upon by an expert."

Portier's reasoning MAY be the basis for his opinion on general causation. Portier's Bradford-Hill analysis is "based on reasons supported by the material on which the expert

relies." The analysis of Neugut's general causation opinion also applies to Portier – Portier can consider non-use, PPI use, and H2RA comparisons, can conclude that risk ratios consistently above 1.0 suggest general causation, and can opine that confidence intervals of 95% below 1.0 do not preclude use of the data.

Portier MAY reasonably rely on the animal studies showing that NDMA causes cancer. (DX37, Portier Report at 23-24, 32-33, 41-42, pages 867-868, 876-877, 885-886.) Portier reviewed animal studies that show NDMA is correlated with a variety of cancers. That noted, Portier did not review any animal studies on the specific issue of whether NDMA is correlated with bladder cancer. Portier testified: "my current recollection is that there are no bladder tumor positive animal studies." (DX2, Portier Depo at 159, page 72.) Portier testified that he asked plaintiff's counsel whether there were animal studies about whether exposure to ranitidine was linked to cancer but that he was not provided any such studies. (DX2, Portier Depo at 165-166, page 73-74.) Portier apparently did not independently look for any animal studies. The court finds that Portier could reasonably rely on animal studies showing that NDMA causes cancer adequately reason that NDMA likely causes bladder cancer in humans.

Portier MAY reasonably rely on the mechanistic studies showing that NDMA causes cancer. (DX37, Portier Report at 42-43, pages 886-887.) The Portier Report states: "NDMA is mutagenic and/or genotoxic (depending on the assay used) in virtually all systems tested." The Portier report states: "The principal DNA adduct formed following exposure to NDMA is N7-methylguanine (representing about 65% of all adducts formed initially upon exposure); … Although there appears to be no direct relationship between the formation of N7-methylguanine and tumor development, the formation and persistence of O6-methylguanine molecules have been shown to be associated with both the carcinogenicity and mutagenicity of NDMA."

Portier's Report then turns to whether the drug ranitidine (as opposed to the chemical NDMA) causes cancer in humans.

Portier MAY testify that ranitidine causes cancer in humans. Portier considers many of the epidemiological studies that Neugut considered – Wang (2022), Cardwell (2021), Braunstein (2021), Norgaard (2021), Iwagami (2021), McDowell (2021), Yoon 2021), Kantor 2021), Mohy-ud-din (2020), and Habel (2000). (DX37, Portier Report at 43-48, pages 887-892.) Portier discusses the Mohy-ud-din (2020) study, which has a risk ratio of less than 1.0 and states: "Because this is an abstract, it is very limited in it's presentation, it does not describe any adjustments for confounders, and it has confounders that clearly could affect ORs, it's use in evaluating cancer risks from ranitidine is extremely limited." (DX37, Portier Report at 47, pages 891.)

As with Neugut, Portier's forest plot shows that in comparisons between ranitidine and non-use, PPIs, and H2RA blockers that all studies have a risk ratio above 1.0 and several have confidence levels are above the 1.0 point. (DX 121, page 3073.) As with Neugut, Portier is an expert on general causation, not specific causation, so the risk ratios of consistently above 1.0 support his conclusion that NDMA creates an increased risk of bladder cancer.

Portier's Bradford-Hill reasoning MAY be the basis for his opinion. (DX 37, Portier Report at 65-70, pages 909-914.)

JAMESON

The Motion of Defendants to exclude testimony of Jameson is DENIED.

Jameson is a chemist and toxicologist. Jameson prepared a report. (DX 33, Jameson Report, pages 589-750.) Jameson was deposed. (Jameson Depo, DX4, pages 117-125.)

Jameson was "asked to provide my expert opinions regarding ranitidine's ability to form N-nitrosodimethylamine (NDMA) both exogenous and endogenously and the carcinogenic potential of NDMA and ranitidine." (DX 33, Jameson Report p1, page 592)

Jameson's opinion is: "it is my opinion to a reasonable degree of scientific certainty that ranitidine is a human carcinogen. I also conclude to a reasonable degree of scientific certainty that ranitidine causes cancer, particularly bladder cancer, in humans at real world exposure levels and conditions. (DX33 Jameson Report p1, page 592.) Jameson has the opinion that ranitidine can degrade to NDMA out of the body (exogenously) and convert in the body (endogenously). (DX33, Jameson Report p7-25, page 599-616.)

Jameson MAY testify that ranitidine can degrade to NDMA outside the body. Jameson's opinion that ranitidine degrades to NDMA during transport/storage out of the body (exogenous) (1) is supported by information "of a type that reasonably may be relied upon by an expert" and (2) is based on adequate reasoning. Jameson relies on "results from several labs including Sanofi, Glaxo Smith Kline, the FDA, and Emery who used a LC-MS method to determine NDMA in ranitidine" and to Abe (2020). (DX 33, Jameson Report at 10-12, page 601-603.) Jameson's reasoning is adequate.

Jameson MAY testify that ranitidine creates NDMA inside the body. Jameson's opinion that ranitidine creates NDMA in the body (endogenous) (1) is supported by information "of a type that reasonably may be relied upon by an expert" and (2) is based on adequate reasoning. Jameson relies on peer reviewed published studies that suggest that ranitidine converts to NDMA in the body. (DX 33 Jameson Report at 12-22, page 603-613.) Jameson's reasoning is adequate. Jameson's opinion is limited. Jameson states: "The available literature that ranitidine could be a potential source of NDMA creation in the body is not consistent" and "Bottom line, the data for

NDMA formation after consumption of ranitidine is not as strong as the data regarding the exogenous formation of NDMA in ranitidine." (DX 33, Report at p12, 22, page 603, 613.) As with Neugut, the expert offers a limited opinion, and that limited opinion is admissible evidence.

Jameson MAY testify that NDMA can cause cancer in humans. Jameson relies on epidemiology, animal studies, and mechanistic studies, and then applies the Bradford-Hill analysis. (Jameson Report p26, page 617.)

Jameson MAY reasonably rely on the animal studies to determine whether NDMA the chemical causes cancer in animals. (Jameson Report p62-66, page 653-657.)

Jameson MAY reasonably rely on mechanistic studies to determine whether NDMA the chemical causes cancer. (Jameson Report p66-69, page 657-660.)

Jameson's Bradford-Hill reasoning MAY be the basis for his opinion that NDMA causes cancer. (Jameson Report p69-72, page 660-663.) Jameson's Bradford-Hill analysis is "based on reasons supported by the material on which the expert relies."

Jameson then turns to whether Ranitidine causes cancer in humans.

Jameson MAY testify that ranitidine causes cancer in humans. Jameson considers many of the epidemiological studies that Neugut and Portier considered: the cohort studies of Habel (2000), Michaud (2004), Kantor 2021), Yoon (2021), Adami (2021), Norgaard (2021), Iwagami (2021), Kumar (2021) and the case-controlled studies of Cardwell (2021), McGwin (2021), Mathes (2008), Braunstein (2021). Jameson did not consider Wang (2022), McDowell (2021), or Mohy-ud-din (2020). (Jameson Report p92, page 683.)

Jameson concludes: "I conclude there is sufficient evidence for the carcinogenicity of ranitidine in humans based on the positive association observed between ranitidine exposures and cancer at real world exposure levels, and that a causal interpretation is creditable. I also

conclude that there is sufficient evidence for the carcinogenicity of ranitidine based on the positive association observed between ranitidine consumption and bladder cancer and esophageal cancer at real world exposure levels, and that a causal interpretation is creditable." (DX 33, Jameson Report at 93, page 684) As with Neugut and Portier, Jameson's opinion is that Ranitidine causes bladder cancer in humans generally and therefore the epidemiology does not need to have the higher risk ratio that is required for a specific causation opinion.

Jameson's Bradford-Hill reasoning MAY be the basis for his opinion that ranitidine causes cancer. (DX 33, Jameson Report at 96-99, page 687-690.) Jameson walks through the Bradford-Hill analysis. Jameson's Bradford-Hill analysis is "based on reasons supported by the material on which the expert relies."

SPECIFIC CAUSATION

The experts on specific causation (Boyd and Conry) offer opinions that Goetz's ingestion of ranitidine caused Goetz to develop bladder cancer. Boyd and Conry used a differential diagnosis for specific causation. A differential diagnosis involves first identifying all the potential causes of an illness and then excluding the potential causes until only one or a few diagnoses are left. This is an established methodology for specific causation. (*Pilliod v. Monsanto Company* (2021) 67 Cal.App.5th 591, 623; *Johnson & Johnson Talcum Powder Cases* (*Echeverria*) (2009) 37 Cal. App. 5th 292, 327-331; *Cooper v. Takeda Pharmaceuticals America, Inc.* (2015) 239 Cal.App.4th 555, 565.)

Differential diagnosis is, almost by definition, not an exact analysis given that it relies on the inference that if most of the identified potential causes are not probable, then the last

remaining potential cause is probable. There are two aspects to the differential diagnosis analysis – the inclusion and the exclusion.

CONRY

The Motion of Defendants to exclude testimony of Conry is DENIED.

Conry is a medical oncologist. Conry prepared a 12-page report with 27 footnotes. (Conry Report DX38 pages 946-963.) (See also DX 86, page 2296 [Conry CV].) Conry was deposed. (Conry Depo, DX 124, pages 3335-3377.)

Conry was asked to assume that ranitidine use is a risk factor for the development of bladder cancer, he assessed peer-reviewed scientific literature, he reviewed Goetz's medical history, and he considered the Emery Pharma lab tests on Goetz's four pills. Boyd conducted a differential diagnosis. Conry's opinion is that "Goetz's decades long use of Zantac/ranitidine contaminated with NDMA was likely a substantial contributing factor in causing his bladder cancer." Conry has this opinion on specific causation "to a reasonable degree of medical certainty." (DX 38, Conry Report at pages 947, 957.)

The court starts with "inclusion." The first aspect of "inclusion" is that the expert must have a reasoned opinion that there is general causation.

The court does not decide whether Conry may reasonably rely on the general causation opinions of Neugut, Portier, and Jameson. The Conry Report states "For the purpose of this report, I have been asked to assume that ingestion of Zantac contaminated with NDMA is a known risk factor for bladder cancer." (DX 38, Conry Report, page 952.) The opinions of Neugut, Portier, and Jameson appear to be litigation quality opinions and not professional scientific quality opinions.

Conry MAY reasonably rely on the medical literature on bladder cancer, peer reviewed studies on NDMA, and on peer reviewed studies on ranitidine. Conry prepared a 12-page report with 27 footnotes referencing peer reviewed scientific articles. The Conry Report states, "Risk factors were assessed based upon peer-reviewed literature and other reliable scientific publications" and that when determining probable causes "I compile a list of known risk factors for a disease outcome based on what is known within the scientific community and within the scientific literature." (DX 38, Conry Report, page 949.) This is information "of a type that reasonably may be relied upon by an expert."

Conry MAY rely on peer reviewed epidemiological studies related to both NDMA and bladder cancer and ranitidine and bladder cancer. The Conry Report considered Jaksyzn (2020), deVocht (2009), Hidajat (2019), Cardwell 2021), and Habel (2000). (DX 38, Conry Report, pages 952, 962-963.)

As with Neugut, Conry MAY reasonably rely on the epidemiological studies of rubber workers to determine whether NDMA at certain doses causes cancer in humans. Conry considered deVocht (2009) and Hidajat (2019). These showed correlation between exposure to *NDMA* and bladder cancer. These did not show correlation between consumption of *ranitidine* and bladder cancer.

As with Neugut, Conry MAY reasonably rely on the epidemiological studies of diet to determine whether NDMA at certain doses causes cancer in humans. Conry considered Jakszyn (2011). This showed correlation between exposure to NDMA and bladder cancer. This did not show correlation between consumption of ranitidine and bladder cancer.

Conry MAY rely on Habel (2000) for inclusion/general causation. This is a study comparing ranitidine with a H2RA blocker (Cimetidine) and finding HR=1.56 (0.745-3.30). The

Conry Report in footnote 26 states that it relied on the Habel study. The Habel study is matter that reasonably may be relied upon by an expert evaluating whether ranitidine causes bladder cancer. The Habel study supports inclusion (general causation) but not specific causation because the Habel study does not show a significant correlation between cimetidine or ranitidine and bladder cancer. The Habel study states: "While there were very modest increases and decreases in risk for some cancer sites among cimetidine users, most were within the limits of chance given no true association. Furthermore, similar risks of these cancers were also observed among ranitidine users." (DX Habel Report, page 1838.)

Conry MAY rely on Cardwell (2021) for inclusion/general causation. (DX 46.) The Cardwell study is a case control study that is based on years of medical records. The Conry Report in footnote 25 states that it relied on the Cardwell study. The Conry Report's analysis expressly relies on the Cardwell study. (DX 38, Conry Report at 11, page 957.) The Cardwell study is matter that may reasonably be relied upon by an expert" evaluating whether ranitidine causes bladder cancer.

Conry's reasoning based on the Cardwell study DID employ "the same level of intellectual rigor that characterizes the practice of an expert in the relevant field." (*Sargon*, 55 Cal.4th at p. 772.) The Cardwell study at Table 3 compared non-users, PPI users, and H2RA users with ranitidine users and found increased risk of bladder cancer for ranitidine users. The Cardwell study compared ranitidine users who took more than 1,095 Defined Daily Doses ("DDD") representing 3 years of ranitidine use with non-users, PPI users, and H2Ra users and found increased risk of bladder cancer for ranitidine users. (DX 46, Cardwell study, page 1760.)

The court finds that Conry's analysis of inclusion/general causation when considering the Habel and Cardwell studies DID apply reasoning and an appropriate "level of intellectual rigor."

As with Neugut and Portier, Conry can consider non-use, PPI use, and H2RA comparisons, can conclude that risk ratios consistently above 1.0 suggest general causation, and can opine that confidence intervals of 95% below 1.0 do not preclude use of the data.

The second aspect of "inclusion" is that the expert must have a reasoned opinion that there is inclusion for this specific person. The specific inclusion analysis starts with the dose of the exposure. "[T]he dose makes the poison" and an expert must consider "the possibility that exposure may not cause a disease when the exposure is below a threshold level." (*People v. Brown* (Cal. 2023) 2023 WL 2319306 at *7; *Lockheed Litigation Cases* (2005) 126 Cal.App.4th 271, 23 Cal. Rptr. 3d 762, 779 [superseded].)

Conry MAY rely on the Bose Report and the Emery Pharma lab reports of the dose of NDMA in the four Goetz pills despite the age of the pills at the date of testing. The Conry Report states: "Four different forms of ranitidine (150mg) in Mr. Goetz's possession were analyzed for NDMA content and each contained NDMA in amounts ranging from 470 ng to 2994 ng per pill, many fold in excess of the FDA "reasonably safe for human ingestion" amount of 96 ng."" (DX 38, Conry Report at 11, page 957.) This is a reference to the Bose Report. (DX36, Bose Report at 840.) Conry's opinion could reasonably consider the tests of the four pills in the Bose Report even though the Emery Pharma tested pills that were expired by more than one year if Conry made some reasoned analysis of how the pills would have likely degraded between the date when Goetz consumed similar pills and the date of the testing. The court could locate no testimony by Conry on that issue,[8] but it might be an area of direct and cross examination at trial.

[8] There is evidence of the NDMA dose in unexpired pills. (E.g., DX 109, Emery pre-litigation tests.) But it does not appear that Conry was asked about whether consumption at that dose would lead him to "include" NDMA as a potential cause of Goetz's bladder cancer.

Conry MAY rely on the Bose Report and the Emery Pharma lab reports of the dose of NDMA in the four Goetz pills despite the fact that they were generic pills. (DX 38, Conry Report, page 957.) As discussed above in the context of Bose, the Emery Pharma test results of Goetz's pills are admissible evidence that is in the nature of a scientific measurement.

Conry MAY testify that Goetz was exposed to a dose of NDMA that was correlated to bladder cancer. The Conry Report states: "Estimates of Mr. Goetz's NDMA exposure place him in the highest risk category according to the Cardwell report from 2021 indicating a fully adjusted hazard ratio of 1.43 after correcting for all other known risks." (DX 38, Conry Report, page 957.) At deposition, Conry was referred to his report and he stated that he considered the exposure dose of NDMA in the Hidajat rubber worker study, did a qualitative (not quantitative) comparison to the exposure dose for Goetz, made a reasoned analysis of the distinction between oral consumption and inhaled consumption, and concluded that Goetz's exposure to NDMA was in the highest exposure quartile in the Hidajat study. (DX 38, Conry Report at 11, page 957.) (DX 124, Conry Depo at 172-176, page 3352.)

Conry MAY reasonably extrapolate the Cardwell study data about ranitidine use for three years (1,095 Daily Defined Doses) to Goetz's 25 years of ranitidine use. (DX 46, Cardwell Study.) The reasonableness of that extrapolation was the subject of argument at the hearing. (Pltf 3/2/23 slides 154, 155; Def 3/9/23 slides 44 and 45) The parties can address the reasonableness of that extrapolation on direct and cross-examination.

Conry MAY reasonably rely on Goetz's medical history, which is factual information. (DX 38, Conry Report, pages 952-954.) This is information "of a type that reasonably may be relied upon by an expert."

The court finds that Conry's differential diagnosis reasoning MAY be the basis for his opinion. Conry applied the established differential diagnosis. (DX 38, Conry Report, page 949.)

Regarding inclusion, Conry MAY include ranitidine as a specific risk factor for the development of bladder cancer in Goetz. Conry considered that Goetz consumed ranitidine daily from some date in the range of 1987-1996 through 2020, which is a minimum of 24 years. Conry did apply the same "level of intellectual rigor" in his analysis and reasoning that an oncologist would be expected to apply in their professional capacity.

Regarding exclusion, Conry had a reasoned basis to exclude age or to conclude that age was sufficiently minimal that there was likely no causal connection. Goetz was 60 when he got bladder cancer and the average age for diagnosis is 65.

Regarding exclusion, Conry had a reasoned basis to exclude cigarette smoking or to conclude that the smoking was sufficiently minimal and distant in time that there was likely no causal connection.

Regarding exclusion, Conry had a reasoned basis to exclude exposure to industrial chemicals or to conclude that the exposure was sufficiently minimal that there was likely no causal connection.

Regarding exclusion, Conry had a reasoned basis to exclude chronic bladder infection, cancer treatment, history of bladder cancer, arsenic exposure, pioglitazone exposure, aristolochic acid exposure, diet, and obesity, because none appear relevant to Goetz.

Regarding exclusion, the Conry Report did not address the risk of bladder cancer from random mutations or idiopathic causes. The case law recognizes that science and medicine cannot always identify what caused a cancer. (Pilliod, 67 Cal.App.5th at 625 [idiopathic causes];

Echeverria, 37 Cal.App.5th at 330-331 [idiopathic causes]; *Chapman v. Procter & Gamble* (11th Cir. 2014) 766 F.3d 1296, 1311 [idiopathic causes].)

Conry addressed idiopathic causes at deposition. Conry testified that "There's not a test you can do on the bladder pathology to say it was caused by … you name the factor," that "spontaneous or DNA replication, random DNA replication errors" can "contribute to a cancer, "that he made no attempt to "quantify what the contribution is to bladder cancer of cancers that are caused by spontaneous replication errors," and that it is "impossible" to "rule out" random mutations as a potential cause of Plaintiff's bladder cancer. (DX124, Conry Dep. at 220, 233-234, 238, pages 3357-3360.) The Conry testimony suggest that random mutations or idiopathic causes is a recognized and omnipresent risk factor even if it is difficult to quantify.

The evidence and argument suggest that it might be difficult to distinguish between dietary cause and idiopathic case. The report by plaintiff expert Jameson states: "It is estimated that the average adult consumes 100 to 110 ng of NDMA daily in the water and food supply." (DX33, Report p22 page 613 [citing White (2020)].) The report by defendant expert Zamboni states: "the estimated total exogenous NDMA exposure from diet ranges from 60 ng to more than 1000 ng per day." (DX 123, Zamboni Report at 9, page 3214.) Given the potential fluctuations in the diets of the average person, it might be difficult to determine whether any given bladder cancer was caused by genetic mutation, routine diet, or other background exposure. That was a topic of argument at the hearings and can be the subject of direct and cross examination at trial.

BOYD

The Motion of Defendants to exclude testimony of Boyd is DENIED.

Boyd is a medical oncologist. Boyd prepared a 21-page report with 108 footnotes referencing peer reviewed scientific articles. (Boyd Report DX130, pages 3475-3504.) Boyd was deposed. (Boyd Depo, DX8 and 126, pages 208-239, 3392-3395.)

Boyd was asked to assume that ranitidine use is a risk factor for the development of bladder cancer, he reviewed medical literature on whether ranitidine use is a risk factor for the development of bladder cancer, he reviewed Goetz's medical history, and he reviewed the lab tests on Goetz's four pills. Boyd conducted a differential diagnosis. Boyd's opinion is that "To reasonable medical certainty ... Mr. Goetz's urothelial bladder carcinoma was caused by his long-term exposure to NDMA from his Zantac/ranitidine intake; but for his NDMA exposures, Mr. Goetz would not have developed urothelial carcinoma." (DX 130, Boyd Report at 21, page 3495.)

The court starts with "inclusion." The first aspect of "inclusion" is that the expert must have a reasoned opinion that there is general causation.

The court does not decide whether Boyd may reasonably rely on the general causation opinions of Neugut, Portier, and Jameson. The Boyd Report states both "I have been asked to assume that ranitidine (Zantac) use is a risk factor for the development of bladder cancer." (DX 130, Boyd Report, at 3487.) The opinions of Neugut, Portier, and Jameson appear to be litigation quality opinions and not professional scientific quality opinions.

Boyd MAY reasonably rely on the medical literature on bladder cancer, peer reviewed studies on NDMA, and on peer reviewed studies on ranitidine. Boyd testified that he did his own analysis as to whether to consider ranitidine as a risk factor for the development of bladder cancer." (DX 8, Boyd Depo at 349, page 236.) Boyd prepared a 21-page report with 108

footnotes referencing peer reviewed scientific articles. (Boyd Report DX130, pages 3475-3504.) This is information "of a type that reasonably may be relied upon by an expert."

Boyd MAY rely for its general inclusion/general causation opinion on peer reviewed epidemiological studies related to ranitidine and bladder cancer. The Boyd Report considered (Habel (2000), Kantor (2021), Norgaard (2022), Braunstein (preprint), Cardwell (2021), and Yoon (2021). (DX 130, Boyd Report pages 12-13 and footnotes 100-106, page 3486-3487.) The court reviews the studies.

1. Habel (2000). Study comparing ranitidine with a H2RA blocker (Cimetidine) and finding HR=1.56 (0.745-3.30). The Habel study is matter that may reasonably be relied upon by an expert" evaluating whether ranitidine causes bladder cancer.
2. Kantor (2021). Comparing ranitidine with PPI users and finding HR=1.30 (0.69-2.46). Comparing ranitidine with non-users users and finding HR=1.22 (0.74-2.01). The Kantor study is matter that may reasonably be relied upon by an expert" evaluating whether ranitidine causes bladder cancer.
3. Norgaard (2021). Comparing ranitidine with H2RA famotidine users and finding HR=1.11 (0.95-1.29). Comparing ranitidine with PPI-users users and finding HR=1.24 (1.04-1.48). The Norgaard study is matter that may reasonably be relied upon by an expert" evaluating whether ranitidine causes bladder cancer.
4. Braunstein (2021). This article is a preprint, which means it has not been subject to peer review. The Boyd report states: "For bladder cancer, ranitidine use was associated with an odds ratio of 1.58." The Braunstein study is unpublished and is NOT a matter that may reasonably be relied upon by an expert."

5. Cardwell (2021). The Cardwell study compared ranitidine users with non-users, compared ranitidine users with PPI-users, and compared ranitidine users with H2RA users. The Cardwell study is matter that may reasonably be relied upon by an expert" evaluating whether ranitidine causes bladder cancer.

6. Yoon (2021). Comparing ranitidine with H2RA famotidine and finding HR=1.41 (0.88-2.24). The Yoon study concludes: "There was no statistical difference in the overall cancer risk between the ranitidine and the famotidine groups." (DX59, Yoon study at 4, page 1962.) The Boyd report states: "[The Yoon study] found no statistical significance in overall cancer risk between the two groups. … Although statistical significance was not reached, [of all the cancers studied] bladder cancer had the highest hazard ratio of 1.41." (DX 130, Boyd Report, page 3487.) The Yoon study is matter that may reasonably be relied upon by an expert" evaluating whether ranitidine causes bladder cancer.

The court finds that Boyd's analysis of general inclusion/general causation DID apply reasoning and an appropriate "level of intellectual rigor" when considering general inclusion/general causation. As with Neugut and Portier, Boyd can consider non-use, PPI use, and H2RA comparisons, can conclude that risk ratios consistently above 1.0 suggest general causation, and can opine that confidence intervals of 95% below 1.0 do not preclude use of the data. Unlike Neugut and Portier, Boyd did not rely on rubber worker or dietary studies to establish that NDMA increases the risk of bladder cancer.

The second aspect of "inclusion" is that the expert must have a reasoned opinion that there is inclusion for this specific person. The specific inclusion analysis starts with the dose of the exposure.

Boyd MAY rely on peer reviewed studies indicating that ranitidine can degrade into NDMA at high temperatures and high humidity. Boyd states: "*Abe, et al.*, assessed the effect of high temperature storage on the stability of ranitidine and its potential formation of NDMA, … These findings highlighted the important role of storage conditions, particularly temperature and moisture, in NDMA formation …" (DX 130, Boyd Report page 3485.) (See also PX 19, Abe (2020).)

Boyd MAY rely on the Bose Report and the Emery Pharma lab reports of the dose of NDMA in the four Goetz pills despite the age of the pills at the date of testing. (DX 130, Boyd Report at 19, page 3493.) The Boyd Report states: "4 separate ranitidine tablets that Mr. Goetz had purchased prior to the recall were tested for NDMA. … Although these pills were expired at the time of their testing, they reflect highly elevated levels of NDMA, far in excess of any safe regulatory limit and indicate the fundamental instability of the product to degrade into NDMA in regular transport and storage." (DX 130, Boyd Report p19, 20, page 3493, 3494.) This is a reference to the Bose Report. (DX36, Bose Report at 840.) As with Conry, Boyd's opinion could reasonably consider the tests of the four pills in the Bose Report even though the Emery Pharma tested pills that were expired by more than one year if Boyd made some reasoned analysis of how the pills would have likely degraded between the date when Goetz consumed similar pills and the date of the testing.

Boyd MAY rely on the Bose Report and the Emery Pharma lab reports of the dose of NDMA in the four Goetz pills despite the fact that they were generic pills. (DX 130, Boyd

Report p19, page 3493.) As discussed above in the context of Bose and Conry, the Emery Pharma test results of Goetz's pills are admissible evidence that is in the nature of a scientific measurement.

Boyd MAY testify that Goetz was exposed to a dose of NDMA that was correlated to bladder cancer. The Boyd Report states: "[The four tested pills] reflect highly elevated levels of NDMA … and indicate the fundamental instability of the product to degrade into NDMA in regular transport and storage. … Mr. Goetz thus likely had significant levels of this carcinogen present in his own medication during his 33 years of use." (DX 130, Boyd Report p20, page 3494.)

At deposition, Boyd was asked whether he calculated Goetz's dose and acknowledged that he did an assessment but not a calculation:

> Q: … did you do a specific calculation to document his -- his exposure to NDMA from ranitidine?
>
> A: It is a range of exposures because of the uncertainty with each tablet he took, the duration he took it in. We know that there is a range of levels that were in ranitidine. So it is very hard to do a full calculation. …
>
> A: I think I may have done a broad assessment of levels, but it is a wide range because, as you know, … these were pills that he had that might have expired, but the level of NDMA in the pills were widely disparate in terms of amount per pill. So it is very hard knowing they are in there and there is significant NDMA in the ranitidine -- to do a dose calculation would be more difficult.

(Boyd Depo, DX 8, p 152-153, pages 216-217.) Boyd's assessment of the Goetz dose is reasonable, but might be the subject of direct or cross-examination at trial.

Based on the assessment of the Goetz dose, Boyd concluded that Goetz was in a "high exposure group," compared Goetz's dose with the exposure doses in the Cardwell ranitidine study and the Hidajat rubber worker study, and made a conclusion about specific inclusion. (DX 130, Boyd Report p20, page 3494.) (See also Boyd Depo, DX8 and 126, pages 3394 -239, 3394.) The Boyd report states: "As discussed by Cardwell, there was a significant increased risk of bladder cancer after 3+ years of ranitidine use (1.43, 95% CI 1.05-1.94). … Based on Mr. Goetz's use of Zantac/ranitidine, he would fall into these highest exposure groups." (DX 130, Boyd Report 20, page 3494.) The Boyd Report, like the Conry report, considered the estimated Goetz dose and then evaluated Goetz's risk based on the data comparing 1,095 ranitidine DDDs (3-year use) with no use rather than evaluating Goetz's risk based on the data comparing 1,095 ranitidine DDDs (3-year use) with H2RA use. Boyd's reasoning is adequate.

The court finds that Boyd MAY reasonably rely on Goetz's medical history, which is factual information. (DX 130, Boyd Report at 13-14, pages 3487-3488.) This is information "of a type that reasonably may be relied upon by an expert."

The court finds that Boyd's differential diagnosis reasoning MAY be the basis for his opinion. Boyd applied the established differential diagnosis. (DX 130, Boyd Report at 4-9, pages 3478-3483.)

Regarding inclusion, Boyd MAY include ranitidine as a specific risk factor for the development of bladder cancer in Goetz. Boyd considered that Goetz consumed ranitidine from the late 1980s through 2020, which 33 years and consumed it daily from 1995 to 2020, which is 25 years. (DX 130, Boyd Report at 14, 19, pages 3488, 3493.) Boyd applied an appropriate "level of intellectual rigor."

Regarding exclusion, Boyd had a reasoned basis to exclude age, gender, or heredity or to conclude that those factors were sufficiently minimal that there was likely no causal connection. Goetz was a white male at age 60 when he got bladder cancer and the average age for diagnosis in that group is 65. That noted, the Boyd deposition suggests that Boyd agreed that in Western populations genetic factors play a role in 7 percent of bladder cancers. (DX 8, Boyd Depo at 142, page 215.)

Regarding exclusion, Boyd had a reasoned basis to exclude cigarette smoking or to conclude that the smoking was sufficiently minimal and distant in time that there was likely no causal connection. Goetz smoked 5-6 cigarettes per day from age 16-17 until age 22. Boyd states: "There is evidence that risk of bladder cancer following cessation approaches baseline risk 20 years after cessation." (DX 130, Boyd Report at 18, page 3492.)

Regarding exclusion, Boyd had a reasoned basis to exclude exposure to industrial chemicals or to conclude that the exposure was sufficiently minimal that there was likely no causal connection. Boyd states: "Mr. Goetz had no occupational exposures known to impart a risk of bladder cancer." (DX 130, Boyd Report at 16, page 3490.)

Regarding exclusion, Boyd had a reasoned basis to exclude diet or to conclude that the exposure was sufficiently minimal that there was likely no causal connection. Boyd states: "he generally had a healthy diet, with occasional steak and red meat but never daily, … He had very limited intake of processed meats, predominantly on special occasions including rare intake of hot dogs, bacon, ham, and sausage." (DX 130, Boyd Report at 17, page 3491.)

Regarding exclusion, Boyd had a reasoned basis to exclude other potential risks because none appear relevant to Goetz.

Regarding exclusion, the Boyd Report did not address the risk of bladder cancer from random mutations or idiopathic causes. Boyd addressed idiopathic causes at deposition. Boyd testified that just as tobacco use is a leading cause of lung cancer, "environmental exposure plays a disproportionate role" in bladder cancer and that random mutations are the cause of less than 5 percent of bladder cancer. (DX008, Boyd Dep. at 144-145, pages 215.) When pressed on this issue, Boyd repeated "They are environmentally driven diseases" and that "the overwhelming majority of bladder cancers are environmental and not bad luck." (DX008, Boyd Dep. at 260, 359-360, pages 228, 238.) As noted in the context of Conry, the evidence and argument suggest that it might be difficult to distinguish between dietary cause and idiopathic case.

QATO (REGULATORY MATTERS)

The Motion of Defendant to exclude testimony of Qato is GRANTED IN PART.

Qato prepared a report. (DX35.) Qato was deposed. (DX14, 15, 16.) Qato is qualified to provide a summary of the FDA regulatory scheme.

TOPIC #1A. General framework of FDA regulations as it applies to ranitidine (prescription and OTC) since 1983. (DX35, Qato Report a 5-30, pages 790-815.) Qato MAY provide testimony that summarizes and explains the regulatory framework for regulation. Qato may NOT opine whether any defendant failed to comply with any given regulation.

TOPIC #1B. Regulatory History of Prescription and OTC Zantac (Ranitidine). (DX35, Qato Report at 30-, pages 815-818.) Qato MAY provide testimony that summarizes and explains the regulatory history of ranitidine. Qato may NOT suggest any notice for any action of any defendant. Qato may NOT opine whether any defendant failed to comply with any given regulation.

TOPIC #2. Whether GSK was obliged to provide NDMA studies to FDA in 1982. (DX35, Qato Report at 33-35, pages 818-820.) Qato can NOT provide testimony an whether GSK was obliged to provide NDMA studies to FDA in 1982. The Qato report did not examine the 1982 versions of the regulations, but she examined the relevant regulations after preparing her report. Qato MAY provide testimony that summarizes and explains the regulatory framework for regulation. Qato may NOT opine whether any defendant failed to comply with any given regulation.

TOPIC #3. Whether FDA has authority to interfere with independent study. (DX35, Qato Report a 35-36, pages 820-821.) Qato MAY provide testimony about whether the FDA has regulatory authority to promote or discourage publication of articles. Qato may NOT provide testimony on whether the FDA promoted or discouraged publication of any given article.

The briefing suggests that on 2/9/20 the Braunstein study on Zantac and cancer was scheduled to be published, that a privilege log produced in this litigation shows a flurry of activity on 2/9/20, and the article was not published. Qato may NOT offer expert speculation that the FDA interfered with the publication of the Braunstein article. The court does not decide the issue, but notes that the flurry of activity is apparently disclosed in a privilege log. A privilege log is a litigation tool for evaluating the validity of a claim of privilege. It is unclear to the court whether a privilege log would be admissible evidence in a trial on the merits. The court also notes that ranitidine was removed from the market in October 2019, so it is unclear what relevance the matter has to plaintiff's claims.

TOPIC #4. Whether cold chaining of ranitidine was permitted. (DX35, Qato Report at 36-39, pages 821-824.) Qato MAY provide testimony about whether the FDA has regulations that permit or require a defendant to update a label to reflect new information about a drug. Qato

may NOT provide testimony on whether defendants were permitted or required to have instructions to cold chain ranitidine.

TOPIC #5. GSK's obligations under FDA regulations regarding preservation and testing of ranitidine pills the United States, after GSK and FDA recalls. (DX35, Qato Report at 40-42, pages 824-826.) Qato MAY provide testimony about whether the FDA has regulations that require a defendant to preserve or test pills. Qato may NOT provide testimony on whether defendants were required to retain or to test pills. Qato may NOT provide testimony on whether defendants violated any regulation that imposed an obligation to retain or to test pills.

PEASE.

The Motion of Defendants to exclude testimony of Pease is GRANTED.

Pease is an environmental scientist. Pease prepared a report. (DX 34, Pease Report, pages 752-783.) Pease was deposed (DX 7, Pease Depo, pages 193-206.)

TOPIC #1. What Proposition 65 is and the addition of NDMA to list of chemicals known to California to cause cancer. (DX 34, Pease Report at 6-, pages 758-783.) Pease may NOT testify about Proposition 65. The standards for addition to the Prop 65 list are significantly different from the standards for causation in this case. The Proposition 65 "No Significant Risk Level" (NSRL) for NDMA is 0.04 micrograms (40 nanograms) per day, which is the level where a daily intake is associated with a risk of cancer of one-in-100,000.[9] Proposition 65 concerns the levels where a business must disclose a risk for purposes of public health and is significantly different from the standard for establishing general causation.

[9] By way of dicta, the court notes that it would assist the court, and might assist the trier of fact, if the experts and the parties used a consistent unit of measurement rather than using both micrograms and nanograms.

The FDA's acceptable daily intake for NDMA is 0.096 micrograms (90 nanograms) per day, which is a "a theoretically calculated level of approximately 1 in 100,000." The FDA states: "These risk levels represent a small theoretical increase in risk when compared to human overall lifetime incidence of developing any type of cancer, which is greater than 1 in 3. … The use of a numerical cancer risk value (1 in 100,000) and its translation into risk-based doses (TTC) is a highly hypothetical concept that should not be regarded as a realistic indication of the actual risk." (DX 94. FDA M7(R1), page 2548-2549.) (See also 21 CFR 556.3)

The court finds that testimony on the addition of NDMA to the Prop 65 list would not "assist the trier of fact" (Evid Code 801) and would likely confuse the trier of fact (Evid Code 352). (See also *Pilliod v. Monsanto Co.* (Cal Superior 2019) 2019 WL 2158266 at *7-8 [granting motion to exclude Pease testimony on Proposition 65].)

TOPIC #2. Processes of how California derived its daily limit of NDMA. Pease may NOT testify about Proposition 65. Therefore, it is not relevant how California derived its daily limit of NDMA for Proposition 65.

IT IS SO ORDERED.

Dated: March 23, 2023

Hon. Judge Evelio Grillo

Superior Court of California, County of Alameda
Department 21, Administration Building

Case Number: JCCP005150
Case Name: Ranitidine Product Cases

ORDER ON MOTIONS OF DEFENDANTS TO EXCLUDE EXPERT TESTIMONY
(EVID CODE 801/802 AKA SARGON/KELLY MOTIONS)

DECLARATION OF ELECTRONIC SERVICE

I certify that I am not a party to these cases and that a true and correct copy of the foregoing document was served electronically pursuant to Pre-Trial Order No. 8, entered in these coordinated proceedings on September 23, 2021 via the CASE ANYWHERE system. Execution of this certificate occurred at 1221 Oak Street, Oakland, California.

Executed on March 23, 2023

Executive Officer/Clerk of the Superior Court

By *Nicole Hall*
Deputy Clerk